Survivorship care planning for women with a gynecological cancer

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Chapter 1

General Introduction

GENERAL INTRODUCTION

The number of cancer survivors is growing

As populations age, each year more individuals are diagnosed with cancer worldwide.[1,2] In the Netherlands the number of new cancer cases per year has almost doubled from 57 thousand in 1990 to 110 thousand in 2017.[3] Fortunately, survival rates for most cancer types have also increased, due to earlier diagnosis and improved cancer treatments.[4] As a result, a growing number of individuals live years beyond a cancer diagnosis and may ultimately survive the disease. In the Netherlands, there were almost 800 thousand cancer survivors in 2017, which is expected to exceed a million by 2025.[4,5] Using the original definition of the American National Coalition of Cancer Survivorship (NCCS), all individuals who were ever diagnosed with cancer are included as 'cancer survivors'.[6] However, 'cancer survivors' and 'cancer patients' are used interchangeably in this thesis.

Cancer survivors face many long-term issues

Cancer survivors often struggle to continue life after cancer treatment due to physical and psychological effects that persist for extended periods of time, or that develop later in post-treatment life.[7] Long-term and late effects frequently reported by cancer survivors include - but are not limited to - fatigue, pain, sleep problems, cognitive limitations, sexual dysfunction, anxiety and depression.[7,8] These symptoms subsequently translate into challenges such as difficulties in performing daily activities, maintaining social relationships and returning to work, which greatly affect the quality of life of many cancer survivors.[7,9] Hence, survivors report a need for information and support to be able to deal with the many issues related to survivorship.[10-12]

Survivorship care is new and complex

In the past decade there has been an increasing awareness of the growing population of cancer survivors that need appropriate care to manage the issues related to survivorship. At the same time, this growing population puts an increasing pressure on health care resources.[13,14] Therefore, efforts have been made to develop guidelines and models to improve care for cancer survivors while dealing with these challenges.[15] In general, survivorship care starts right after cancer treatment and is provided to individuals that are cancer-free or able to manage chronic or intermittent disease (Fig 1).[16] However, for those with disease progression or a recurrence, it is emphasized that survivorship care and palliative care should be integrated across the cancer care continuum that flows from diagnosis into end-of-life-care.[16,17]

Several models of care have been proposed that aim to incorporate survivorship care into the cancer care trajectory, ranging from one-time consultations by a provider from the oncology team to more extensive multidisciplinary care within the cancer center.[15]

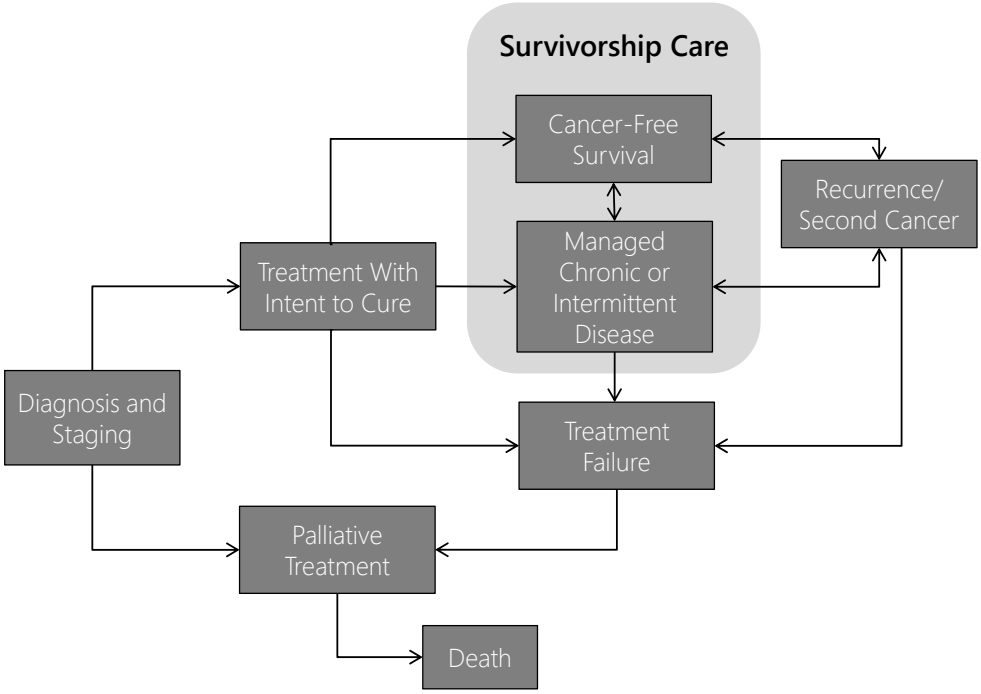

Figure 1: The Cancer Care Trajectory, adapted from the Institute of Medicine, 2006

Although evidence is lacking for any of these survivorship care models[18], the 'shared care model' has been widely endorsed as proposed by the American Institute of Medicine (IOM) and supported by the American Society of Clinical Oncology (ASCO)'.[16] According to this model, cancer survivors are transferred from the oncologist to the primary care physician for the continuation of long-term care, mostly starting from one to two years after diagnosis.[15] However, most practices outside of the United States, including the Netherlands, use a more traditional model in which cancer survivors continue to receive first-line follow-up care, by either their oncologist or oncology nurse, up to five years after diagnosis or longer.[19]

'Survivorship care plans' are widely recommended

A central component of the shared care model that was recommended by the IOM in 2006, is a 'survivorship care plan' (SCP).[16] According to the IOM, all cancer patients completing primary treatment should be provided with an SCP containing a comprehensive care summary including a record of all care received and important disease characteristics, a follow-up care plan including written information on the known and potential late effects of the treatments received, and recommendations for health promotion.[16] A central goal of the SCP is to transfer cancer survivors from cancer treatment to primary care. Therefore, the SCP should not only be provided to the survivor, but also to the survivor's primary

care physician. Following the IOM, several paper and web-based SCP templates have been developed[20-22] and the recommendation has been widely adopted outside of the United States. The Dutch Health Counsel has recommended SCPs for all cancer survivors in the Netherlands since 2007.[23]

The implementation of survivorship care plans is slow

Ever since the first recommendation in 2006, the implementation and dissemination of SCPs has been slow and inconsistent. In the United States, it was estimated that less than a quarter of survivorship care programs provided SCPs in 2011, and less than one out of eight patients received one.[24] Since SCPs were implemented as a care standard by the American Commission on Cancer (CoC) in 2015, the proportion of cancer survivors receiving SCPs in affiliated programs slowly increased to 20% in that year.[25] In Europe, the implementation and receipt of SCPs has not been reported, but the lower endorsement of survivorship care programs in Europe compared to the United States[26] suggests an even lower compliance to SCP guidelines. The main barriers to SCP provision include the limited availability of templates or (electronic) systems to create SCPs and lack of time to provide them.[24,27] The time needed for an oncologist or oncology nurse to create and provide an SCP was estimated to range from 1 to 4 hours.[28-30]

Evidence for the effectiveness of survivorship care plans is limited

As the IOM's recommendation was not evidence-based back in 2006, SCPs have been the center of survivorship research since first recommended. Qualitative studies and observational surveys yielded promising results: survivors found that SCPs were empowering and reassuring, they were more satisfied with care and communication between health care providers, and were more motivated to change their lifestyle.[31,32] Moreover, primary care physicians felt increasingly comfortable in providing continued follow-up care to survivors.[32] However, contrary to initial hopes and expectations, randomized controlled trials (RCTs) failed to identify beneficial effects of SCPs in various patient populations, including breast[33,34], gynecological[28,35,36], colorectal[29] and prostate[37] cancer. Hence, the evidence-base for SCPs is still inconclusive. The one RCT that evaluated SCPs in the Netherlands is the ROGY Care Trial.

The ROGY Care Trial evaluates the impact of automatically generated survivorship care plans

Between 2011 and 2016 the ROGY Care Trial was conducted to assess the effectiveness of automatically generated SCPs on patient and health care provider reported outcomes in ovarian and endometrial cancer.[38] The ROGY Care Trial was the first pragmatic cluster randomized controlled trial that evaluated the effectiveness of SCPs. The pragmatic component allowed individual practices to decide who was providing the SCP (i.e. gynecologist or oncology nurse) and how much time was dedicated to discussion of the

SCP, both maximizing the generalizability to 'real life' clinical practice. The cluster design prevents contamination between the trial arms by randomizing hospitals instead of individual patients.[38] In total, 12 hospitals in the south of the Netherlands were randomized to providing 'SCP care' or 'care as usual'. In the SCP Care arm, SCPs were automatically generated, which minimized the time needed to create and provide the SCP. SCPs were generated by simply clicking a button in the web-based Registration system Oncological GYnecology (ROGY). The SCP contained a treatment summary including information on diagnostic tests, type of cancer, stage, grade, treatment, and contact details of the hospital and specialists, and a tailored follow-up care plan, including detailed information on the most common short- and long-term effects of the treatments received and information about additional support. The oncology providers were instructed to deliver the SCP to the patient in print-form and to at least discuss the most important components, such as the diagnosis, treatments received, and most important side-effects. The effectiveness of the SCP was evaluated in patients, oncology providers and primary care physicians.[38]

The ROGY Care Trial included ovarian and endometrial cancer patients

The ROGY Care Trial included women that were recently diagnosed with ovarian or endometrial cancer and were treated with curable intent. Ovarian and endometrial cancer are the two most common gynecological cancer types and, respectively, the fourth and seventh most common cancer types for women worldwide.[39] In the Netherlands about 2,000 women were diagnosed with endometrial cancer and 1,300 with ovarian cancer in 2017.[40] Ovarian cancer is the deadliest gynecological cancer, with only 38% of patients surviving 5 years after their diagnosis, while this is 80% for endometrial cancer patients.[40] Endometrial cancer is mostly diagnosed at earlier cancer stages (stage I or II) and treated with surgical removal of the uterus, fallopian tube and/or ovary (staging). For aggressive tumors, adjuvant radiotherapy or chemotherapy is considered. At higher stages (stage III or IV) of endometrial cancer, additional surgery (staging and/or debulking) and/or adjuvant radiotherapy or chemotherapy is needed.[41] Similarly, low stage ovarian cancer (I or IIA) can be treated with surgery (staging) only, but ovarian cancer is mostly diagnosed at higher cancer stages (IIB, III or IV) and requires a combination of surgery (staging and debulking) and chemotherapy.[42] Common issues resulting from gynecological cancer treatment include infertility, pain, post-menopausal symptoms, sexual dysfunction, bowel and bladder dysfunction, peripheral neuropathy and fatigue.[43-45] In the Netherlands both ovarian and endometrial cancer patients receive first-line follow-up care until 5 years after diagnosis.[19]

Prior results from the ROGY Care Trial are not conclusive

In the ROGY Care Trial, SCPs were received by 74% of the endometrial cancer patients in the SCP Care arm. In this group SCPs increased the perceived amount of information received, but not the satisfaction with the information and care received. Instead, SCPs

increased concerns about the illness, emotional impact, the symptoms experienced and cancer-related contact with the primary care physician (PCP).[35] However, SCPs seemed helpful for endometrial cancer patients who did not use the internet to look up medical information, comprising two-thirds of the sample.[46] Oncology providers were generally satisfied with the SCP but encountered difficulties in finding the time to provide and discuss it.[47] Only one third of the patients' PCPs received a copy of the SCP, and those who received one reported a desire for a more concise version.[48] Prior publications from the ROGY Care Trial only evaluated the impact of SCPs in endometrial cancer and not yet in ovarian cancer. Therefore, definite conclusions about the effectiveness of SCPs on patient reported outcomes could not be drawn. It also remained unclear why some patients did and others did not receive an SCP, and whether threatening illness perceptions due to the SCP are either harmful or beneficial for the patient. On the one hand, threatening illness perceptions due to the SCP may reflect a more realistic perspective of the disease, which helps to accept future consequences of the disease. On the other hand, SCPs may cause persistent psychological distress by giving rise to more threatening illness perceptions.[49] In view of the poorer prognosis in ovarian cancer, the information provided in the SCP may be perceived as even more threatening by ovarian cancer patients compared to endometrial cancer patients.

Models for 'survivorship care planning' are undefined

In this thesis, 'survivorship care plan' (SCP) refers to the actual document containing written information that is provided to the patient. 'Survivorship care planning' as a broader term refers to the process of information provision in survivorship care, comprising what type of information is provided and when, how and by whom it is provided.[50] There is no "one-size-fits-all" approach for survivorship care planning, and implementation typically depends on the individual practice, the availability of resources and the survivor population. Hence, an major challenge of survivorship care planning is that the entire process has to meet the needs of multiple stakeholders, including the patient, his or her caregivers, and health care providers. Factors contributing to successful survivorship care planning remain undefined.[51,52]

Aims and outline of this thesis

The central goal of this thesis was to understand the impact information provision has on (gynecological) cancer survivors and use our findings to inform future survivorship care planning. The three overall aims were:

1. To assess the impact of survivorship care plans (SCPs) on patient-reported outcomes among ovarian and endometrial cancer survivors in daily clinical practice;
2. To understand the role illness perceptions play in the impact of SCPs;
3. To assess the need for information and care among (gynecological) cancer survivors across the cancer care continuum.

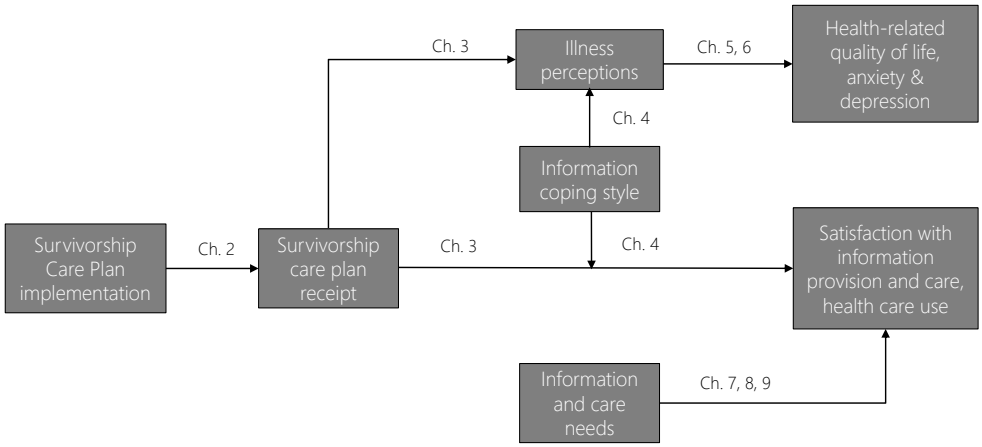

Figure 2: Conceptual framework of the effects of survivorship care plans and information and care needs on patient reported outcomes

A conceptual framework was developed to guide the outline of this thesis, and to describe the effects of SCPs on patient reported outcomes and the mediating and moderating factors influencing the effects (Figure 2). This framework was based on existing behavioral and methodological models, including Leventhals' Self-Regulation Model of Illness[53], Miller's behavioral style scale[54] and Caroll's implementation fidelity framework[55].

Part I: the impact of survivorship care plans

First, according to implementation research, we must assess the degree in which the intervention was delivered as intended (i.e. 'implementation fidelity') before we can evaluate the effectiveness of the intervention.[55,56] Therefore, the aim of **Chapter 2** is to evaluate the degree of SCP receipt in the intervention arm of the ROGY Care Trial and the factors associated with SCP receipt. The main effects of SCPs on patient reported outcomes in ovarian cancer, including satisfaction with information provision and care, health care use and illness perceptions are described in **Chapter 3** and mirror a previous publication from the ROGY Care Trial in endometrial cancer.[35] Further considering that individuals respond differently to health information according to their information coping style, as reported by Miller (1987), **Chapter 4** aims to assess whether the impact of SCPs on the main outcomes in the ROGY Care Trial was moderated by information coping styles. Miller identified two main information coping styles: information seeking ('monitoring') and information avoiding ('blunting').[54,57]

Part II: the role of illness perceptions

According to Leventhal's Self-Regulation Model of Illness (1980), individuals that are confronted with a health threat - such as a cancer diagnosis - develop cognitive and emotional representations of the illness, which through coping responses have an effect on emotional and health outcomes.[53] SCPs may intervene in the pathway illustrated by Leventhal, by increasing threatening illness perceptions. Therefore, the aim of **Chapter 5** is to assess the indirect effects of SCPs on health-related quality of life, anxiety and depression through illness perceptions. In order to further investigate whether 'realistic' information as presented in an SCP is beneficial for cancer survivors, we seek to assess the benefits of 'realistic', 'optimistic' or 'pessimistic' illness perceptions with regard to an individual 's prognosis. This cross-sectional analysis of the PROFILES registry including various cancer diagnoses is presented in **Chapter 6.**

Part III: Information and care needs

In order to define optimized models for survivorship care planning, we aim to assess the information and care needs of cancer survivors across the cancer care continuum. **Chapter 7** concerns survivorship care planning in the year following treatment of gynecological cancer, and describes the perspectives of patients, caregivers and health care providers from an American Academic Medical Center. The aim of **Chapter 8** is to identify subgroups of cancer survivors with distinct patterns of health care needs and factors associated with these patterns, in an American sample of survivors with various non-metastasized cancer types. **Chapter 9** concerns patients with recurrent endometrial or ovarian cancer and describes the differences in satisfaction with information and care before and after diagnosis of a recurrence among patients included in the ROGY Care Trial.

REFERENCES

1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. *Cancer Epidemiology and Prevention Biomarkers*. 2016;25(1):16-27.
2. Hay CM, Courtney-Brooks M, Lefkowits C, Hagan TL, Edwards RP, Donovan HS. Symptom management in women with recurrent ovarian cancer: Do patients and clinicians agree on what symptoms are most important? *Gynecologic oncology*. 2016;143(2):367-370.
3. Netherlands Cancer Registry (NCR). Incidentie alle tumoren. *Cijfers over Kanker* 2018; www.cijfersoverkanker.nl.
4. KWF. *Kanker in Nederland tot 2020, Trends en Prognoses*. 2011.
5. Netherlands Cancer Registry (NCR). Prevalentie alle tumoren. *Cijfers over Kanker* 2018; www.cijfersoverkanker.nl.
6. National Coalition for Cancer Survivorship (NCCS). NCCS Mission. 2018; https://www.canceradvocacy.org/about-us/our-mission/.
7. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *The International Journal of Psychiatry in Medicine*. 2010;40(2):163-181.
8. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. *Cancer*. 2008;112(S11):2577-2592.
9. Wu H-S, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. *Cancer nursing*. 2015;38(1):E29-E54.
10. Geller BM, Vacek PM, Flynn BS, Lord K, Cranmer D. What are cancer survivors' needs and how well are they being met? *The Journal of family practice*. Oct 2014;63(10):E7-16.
11. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Supportive Care in Cancer*. 2009;17(8):1117-1128.
12. Kent EE, Arora NK, Rowland JH, et al. Health information needs and health-related quality of life in a diverse population of long-term cancer survivors. *Patient education and counseling*. 2012;89(2):345-352.
13. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment–psychosocial and behavioural issues in cancer survivorship research and practice. *European Journal of Cancer Supplements*. 2014;12(1):54-64.
14. Nekhlyudov L, Ganz PA, Arora NK, Rowland JH. Going Beyond Being Lost in Transition: A Decade of Progress in Cancer Survivorship. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. Jun 20 2017;35(18):1978-1981.
15. Oeffinger KC, McCabe MS. Models for delivering survivorship care. *Journal of Clinical Oncology*. 2006;24(32):5117-5124.
16. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
17. Hui D, Bruera E. Integrating palliative care into the trajectory of cancer care. *Nature Reviews Clinical Oncology*. 2016;13(3):159-171.
18. Recklitis CJ, Syrjala KL. Provision of integrated psychosocial services for cancer survivors post-treatment. *The Lancet Oncology*. 2017;18(1):e39-e50.
19. Oncoline. Herstel na Kanker, Landelijke Richtlijn, versie 1.0. www.oncoline.nl: Oncoline; 2011.
20. Oncolink. Oncolife Survivorship Care Plen. *Livestrong Care Plan* 2018; http://www.livestrongcareplan.org/.
21. Oncology ASoC. ASCO Cancer Treatment and Survivorship Care Plans. *Survivorship* 2018; https://www.cancer.net/survivorship/follow-care-after-cancer-treatment/asco-cancer-treatment-and-survivorship-care-plans.
22. Survivorship NCfC. Examples of Cancer Care Plans. 2018; https://www.canceradvocacy.org/resources/planning-your-care/examples-of-cancer-care-plans/.
23. Netherlands HCot. *Follow-up in oncology. Identify objectives, substantiate actions*. The Hague: Health Council of the Netherlands;2007.

24. Birken SA, Mayer DK, Weiner BJ. Survivorship care plans: prevalence and barriers to use. *Journal of cancer education : the official journal of the American Association for Cancer Education.* Jun 2013;28(2):290-296.
25. Miller NS. The Commission on Cancer's survivorship care plan standard: Implementation is underway. American Society of Clinical Oncology; 2017.
26. Rowland JH, Kent EE, Forsythe LP, et al. Cancer survivorship research in Europe and the United States: where have we been, where are we going, and what can we learn from each other? *Cancer.* 2013;119(S11):2094-2108.
27. Dulko D, Pace CM, Dittus KL, et al. Barriers and facilitators to implementing cancer survivorship care plans. *Oncology nursing forum.* Nov 2013;40(6):575-580.
28. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
29. Jefford M, Gough K, Drosdowsky A, et al. A randomized controlled trial of a nurse-led supportive care package (SurvivorCare) for survivors of colorectal cancer. *The oncologist.* 2016;21(8):1014-1023.
30. Spain PD, Oeffinger KC, Candela J, McCabe M, Ma X, Tonorezos ES. Response to a treatment summary and care plan among adult survivors of pediatric and young adult cancer. *Journal of oncology practice.* 2012;8(3):196-202.
31. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
32. Salz T, Oeffinger KC, McCabe MS, Layne TM, Bach PB. Survivorship care plans in research and practice. *CA: a cancer journal for clinicians.* 2012;62(2):101-117.
33. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. *Journal of Cancer Survivorship.* 2015;9(4):683-691.
34. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
35. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
36. de Rooij BH, Ezendam NPM, Nicolaije KAH, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecologic oncology.* May 2017;145(2):319-328.
37. Emery JD, Jefford M, King M, et al. ProCare Trial: a phase II randomized controlled trial of shared care for follow-up of men with prostate cancer. *BJU international.* 2017;119(3):381-389.
38. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2011;12:256.
39. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA: A cancer journal for clinicians.* 2015.
40. IKNL. Prevalentie | Vrouwelijke geslachtsorganen. *Cijfers over kanker* 2018; www.cijfersoverkanker.nl. Accessed 03-04-2018.
41. Oncoline. Initiële behandeling. *Endometriumcarcinoom* 2018; https://www.oncoline.nl/endometriumcarcinoom.
42. Oncoline. Behandeling. *Epitheliaal Ovariumcarcinoom* 2018; https://www.oncoline.nl/ovariumcarcinoom
43. Ferrell B, Smith S, Cullinane C, Melancon C. Symptom concerns of women with ovarian cancer. *Journal of pain and symptom management.* Jun 2003;25(6):528-538.
44. Bradley S, Rose S, Lutgendorf S, Costanzo E, Anderson B. Quality of life and mental health in cervical and endometrial cancer survivors. *Gynecologic oncology.* 2006;100(3):479-486.
45. Abbott-Anderson K, Kwekkeboom KL. A systematic review of sexual concerns reported by gynecological cancer survivors. *Gynecologic oncology.* 2012;124(3):477-489.
46. Nicolaije KA, Ezendam NP, Pijnenborg JM, et al. Paper-Based Survivorship Care Plans May be Less Helpful for Cancer Patients Who Search for Disease-Related Information on the Internet: Results of the Registrationsystem Oncological Gynecology (ROGY) Care Randomized Trial. *Journal of medical Internet research.* 2016;18(7).

47. Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, van de Poll-Franse LV, Kruitwagen RF. Oncology providers' evaluation of the use of an automatically generated cancer survivorship care plan: longitudinal results from the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Jun 2014;8(2):248-259.
48. Ezendam NP, Nicolaije KA, Kruitwagen RF, et al. Survivorship Care Plans to inform the primary care physician: results from the ROGY care pragmatic cluster randomized controlled trial. *Journal of cancer survivorship : research and practice.* Dec 2014;8(4):595-602.
49. van de Poll-Franse LV, Nicolaije KA, Ezendam NP. The impact of cancer survivorship care plans on patient and health care provider outcomes: a current perspective. *Acta Oncologica.* 2017;56(2):134-138.
50. Burbage D. Survivorship Care Planning. *Supportive Cancer Care*: Springer; 2016:97-109.
51. Stricker CT, Jacobs LA, Risendal B, et al. Survivorship care planning after the institute of medicine recommendations: how are we faring? *Journal of cancer survivorship : research and practice.* Dec 2011;5(4):358-370.
52. Parry C, Kent EE, Forsythe LP, Alfano CM, Rowland JH. Can't see the forest for the care plan: a call to revisit the context of care planning. *Journal of Clinical Oncology.* 2013;31(21):2651-2653.
53. Leventhal H, Meyer D, Nerenz D. The common sense representation of illness danger. *Contributions to medical psychology.* 1980;2:7-30.
54. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *Journal of personality and social psychology.* 1987;52(2):345.
55. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework for implementation fidelity. *Implementation science : IS.* 2007;2(1):40.
56. Chaudoir SR, Dugan AG, Barr CH. Measuring factors affecting implementation of health innovations: a systematic review of structural, organizational, provider, patient, and innovation level measures. *Implementation science : IS.* 2013;8:22.
57. Miller SM. Monitoring versus blunting styles of coping with cancer influence the information patients want and need about their disease. Implications for cancer screening and management. *Cancer.* 1995;76(2):167-177.

Part I: the impact of SCPs on patient reported outcomes

Chapter 2

Factors influencing implementation of a Survivorship Care Plan – a quantitative process evaluation of the ROGY care trial

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ABSTRACT

Purpose: to investigate the factors that influence implementation of Survivorship Care Plans (SCPs) in the intervention arm of the ROGY care trial by 1) assessing the level of SCP receipt in the ROGY care trial and 2) identifying patient- and provider-level factors that influence SCP receipt.

Methods: Between 2011 and 2015, a pragmatic cluster randomized-controlled-trial was conducted on the effects of automatically generated SCPs. Endometrial (N=117) and ovarian (N=61) cancer patients were allocated to 'SCP care', as provided by their SCP care providers (N=10). Associations between SCP receipt (self-reported SCP receipt and actually generated SCPs), patient-factors (socio-demographic-, clinical-, and personality factors) and care provider factors (profession, a-priori motivation regarding SCP provision) were tested in univariate analysis. The odds ratios of factors influencing self-reported SCP receipt were estimated with a multivariate regression model.

Results: Of all patients in the SCP care arm (N=178), SCPs were generated by the care provider for 90% of the patients and 70% of the patients reported that they had received an SCP. Patients with older age, ovarian cancer, type D (distressed) personality, and patients that completed the questionnaire a longer period of time after the SCP consult were more likely to report no SCP receipt.

Conclusions: SCP receipt was influenced by patient- but not care-provider factors.

Implications for cancer survivors: Certain patient groups were less likely to report SCP receipt. Whether all patients are in need of an SCP requires further investigation. If they do, more efforts need to be made towards the implementation of SCPs.

INTRODUCTION

In 2006, the American Institute of Medicine (IOM) and the Dutch Health Council advocated Survivorship Care Plans (SCPs) as a standard of care for all cancer patients.[1,2] An SCP is a formal document that is handed to the patient and includes a record of all care received, important disease characteristics of the patient, short- and long term effects of the treatments received and information for supportive care services.[1] SCPs aim to promote cancer survivors' follow-up care and outcomes.[1] However, since the IOM's recommendations, implementation and dissemination of SCPs in clinical practice have been low and inconsistent.[3-6]

Our recently published study of the pragmatic cluster-randomized ROGY care trial[7] was accompanied by an editorial declaring the need for more attention for implementation of SCPs.[8] The ROGY Care study contributes to the small number of clinical trials that have evaluated the effects of SCPs on patient reported outcomes.[9-11] Published SCP trials could not draw definite conclusions on SCP effectiveness and highlighted the complexity of SCP implementation.[7,9-11] It is therefore recognized that, alongside investigations of the effectiveness of SCPs, we need to understand how SCPs were implemented and compare implementation strategies between SCP trials.[8,12] The pragmatic nature of the ROGY care trial provides the unique opportunity to evaluate implementation of SCPs in clinical practice.

Evaluations of intervention implementation often include a measure of fidelity - that is, the degree to which an intervention was delivered as intended.[13] The implementation fidelity of SCPs (i.e. the content of the SCP, the coverage of patients that receive SCPs and the frequency of SCP receipt) is expected to have an impact on survivors' outcomes.[8] Subsequently, poor implementation fidelity of SCP care in clinical trials would diminish the observed effects of SCPs, leading to an underestimation of true SCP effectiveness.[13]

Little is known about the factors that influence implementation of SCPs. Current evidence is predominantly based on qualitative studies that focus on system- and organizational level factors that influence SCP implementation, including organizational resources, adequate (electronic) systems, templates and training for SCP use.[3,14-19] A few observational studies have revealed that patients with lower age, non-white race, higher income, higher educational level, better than fair health status, and patients that participated in a trial, more often reported receipt of an SCP.[4,19-21] However, generalizability of these observational studies is limited due to patient selection bias. Furthermore, in these studies only self-reported receipt of SCPs by patients was available.[4,19-21] To our knowledge, no SCP effectiveness randomized controlled trials have yet examined the factors that influence implementation of SCPs.

The ROGY care trial provides longitudinal quantitative data on a wide range of patient-level and provider-level factors, along with both objective and self-reported implementation outcomes of SCPs in routine Dutch clinical practice. Patient-level factors include demographic, clinical and personality characteristics, and provider-level factors include demographic characteristics, profession and opinions regarding SCPs. Understanding factors that promote or inhibit successful implementation of SCPs in the ROGY care trial can support future implementation of SCPs.[8,12]

The aim of the current study is to investigate factors that influence implementation of SCPs in the ROGY care trial by 1) assessing the level of SCP receipt and 2) identifying patient- and provider-level factors that influence SCP receipt.

METHODS

Design

Between April 2011 and October 2015, the pragmatic cluster-randomized ROGY Care Trial was conducted to evaluate the impact of an automatically generated SCP on gynecological cancer patient and health care provider reported outcomes. In the South of the Netherlands, 12 hospitals were randomized to either 'usual care' or 'SCP care'. After initial diagnosis, all endometrial and ovarian cancer patients were invited to participate in the study. Patients were invited with a letter, informed consent form, and questionnaire, sent to the patient by their own gynecologist.[22,23] Follow-up questionnaires were sent directly to the patient at 6, 12, 18 and 24 months after diagnosis. Patients, but not care providers, were blinded to trial assignment. The ROGY care trial was centrally approved by a Medical Research Ethics Committee, as well as by each participating center.[22] The trial design has been described in detail elsewhere.[22] The present study describes the results of implementation fidelity in the intervention arm.

Patients and care providers

Participants include 117 newly diagnosed endometrial and 61 ovarian cancer patients that were in the intervention arm of the ROGY care trial and completed the first questionnaire, and their 10 SCP care providers (i.e., gynecologists, gynecologic oncologists, oncology nurses) in the 6 hospitals of the intervention arm. A follow-up questionnaire was sent to the patients 12 months after diagnosis. Follow-up questionnaires were returned by 68% (N=79) of the endometrial and 57% (N=35) of the ovarian cancer patients. Patient exclusion criteria (i.e., undergoing palliative care or unable to complete a Dutch questionnaire)[22] were minimal to maximize generalizability.[24] All care providers of the intervention arm (N=10) completed a questionnaire before the start of the trial.[25]

Implementation of SCP care

In the hospitals that were allocated to 'SCP care', all care providers attended an instruction evening. The care providers were instructed to provide an SCP to patients after diagnosis and to provide an updated SCP during follow-up visits if applicable (i.e. when there were changes in the cancer, treatment, or oncology provider). In addition, care providers were instructed to send a copy of the SCP to the patient's primary care physician.[26] Practical guidelines were given on the components of the SCP that should minimally be discussed with each patient during the SCP consult (i.e. diagnosis, prognosis, treatment(s), most important side-effects) and how often the SCP should be discussed (shortly after diagnosis and during follow-up visits after 6, 8, 12, 18 and 24 months). Care providers in the SCP care arm were instructed to provide the first SCP at the consultation where the results of histopathology and (adjuvant) treatment plan were discussed, mostly 7-14 days after the operation or biopsy. Because of the pragmatic approach, care providers in the SCP care hospitals were free to choose whether the gynecologist/gynecologic oncologist, and/or oncology nurse provided the SCP, fitting their clinical practice.[22] No other care providers (i.e. medical oncologists or radiotherapists) were involved in the trial because they do not use the registration system through which SCPs were generated.

SCPs could be automatically generated through the web-based 'Registrationsystem Oncological Gynecology' (ROGY), which is used by all participating oncology providers in both arms since 2006. For each patient, a detailed registration is made in a uniform way, including tumor stage and grade, treatment, comorbidity, complications, follow-up, and information about the involved specialists (e.g., gynecologist/gynecologic oncologist, medical oncologist, radiotherapist). For the ROGY care trial, an application was built in ROGY that enables automatic generation of an SCP combining patient and disease data from ROGY. Care providers could generate an SCP by pressing a button in ROGY. This button was only visible for the care providers in the intervention arm.

Survivorship care plan

The SCP was based on the Dutch translation of IOM's SCP template,[27] adjusted to the local situation[28] by a group of gynecologists/gynecologic oncologists, oncology nurses, a radiotherapist, medical oncologist, primary care physician, and patients.[22] Texts of the SCP were based on pilot-tested patient education material from the Dutch Cancer Society. In addition, the SCP was pilot-tested on patients with a low/intermediate educational level to ensure that the SCP was understandable.

The SCP consisted of a tailored treatment summary including information on diagnostic tests, type of cancer, stage, grade, treatment (type, date and specialist), and contact details of the hospital and specialists. The treatment summary contained explanatory notes of the clinical information provided and visual representations of affected organs

and cancer stage. In addition, the SCP contained a tailored follow-up care plan, including detailed information on the most common short- and long-term effects of the treatments received, effects on social and sexual life, possible signs of recurrence and secondary tumors, and information on rehabilitation, psychosocial support, and supportive care services.[22]

Measures

SCP receipt

Receipt of SCPs was assessed by the number of patients for whom SCPs were generated, the number of patients that reported having received an SCP, the number of patients for whom follow-up SCP(s) were generated and the number of patients that reported having received a follow-up SCP. The number of patients of whom (first and follow-up) SCPs were generated was obtained from ROGY. ROGY recorded whether the SCP was generated for the patient by a care provider. Whether the patients actually received the SCP was based on self-report, by asking 'did you receive a survivorship care plan?'. No further explanation about the SCP was given in the questionnaire to avoid feelings of disadvantage in the control arm. Follow-up SCP receipt was assessed by follow-up questionnaires ('how often did you receive a survivorship care plan?'), on 6 and 12 months after diagnosis. Patients that reported (first or follow-up) SCP receipt while no SCP was generated in ROGY were allocated to 'reported no (first or follow-up) SCP receipt', because it was not possible to receive an SCP when not generated.

Patient factors

Age, socio-economic status (SES) and clinical data, such as cancer type, cancer stage and date of diagnosis, were obtained from the Netherlands Cancer Registry (NCR). The NCR routinely collects data on newly diagnosed cancer patients in all hospitals in the Netherlands.[29] SES was based on postal code of the residence area of the patient, combining aggregated individual fiscal data on the economic value of the home and household incomes.[30] SES was categorized into low, medium or high.

Shortly after diagnosis, a first questionnaire was sent to the patient to assess partner status, the number of comorbidities and Type D personality. Partner status was dichotomized (having a partner vs. not having a partner). The number of comorbidities was assessed by the adapted Self-administered Comorbidity Questionnaire (SCQ).[31] Type D (distressed) personality is defined as the joint tendency towards negative affectivity (e.g. worry, irritability, gloom) and social inhibition and has previously been associated with lower perceived receipt of information in cancer patients.[32] Type D personality was assessed by the type-D scale (DS14).[33]

In a follow-up questionnaire 12 months after diagnosis, health literacy was measured by one item of the 5-point Chew's scoring scale ('How confident are you by filling out medical forms?').[34] Low health literacy was defined as being somewhat, a little or not at all confident filling out medical forms, medium health literacy was defined as being quite confident filling out medical forms and high health literacy was defined as being very confident filling out medical forms.[34] Furthermore, the time between SCP consult and completion of questionnaire was calculated by the difference in weeks between first treatment received (obtained from the NCR) and the date of filling out the first questionnaire.

SCP care provider factors

The primary oncology provider (i.e. gynecologist or gynecologic oncologist) that was in charge of the SCP care of the patient, was registered in ROGY. In 3 out of 6 hospitals in the intervention arm, the provision and discussion of the SCP was delegated to an oncology-nurse. Age, sex and motivation of the care providers regarding SCP provision and opinion about SCP benefit were measured by a questionnaire among all care providers before the start of the trial.[25] Motivation regarding SCP provision ('How motivated are you to start using the SCP?') and opinion about SCP benefit ('To what extent do you expect the SCP to affect the patient positively?') were measured on a 10-point scale (strongly disagree – strongly agree).

Statistical analysis

Statistical analyses were conducted using Statistical Analysis System (SAS) version 9.4. (SAS Institute, Cary, NC, 1999). Means with standard deviations (SD) were used to describe normally distributed continuous variables, medians and interquartile ranges (25^{th}-75^{th}) to describe not normally distributed variables and frequencies (N) with percentages (%) to describe categorical variables. All patient- and care provider level factors influencing SCP receipt were assessed in univariate analysis, using independent samples t-tests for normally distributed continuous variables, Mann-Whitney U Test for not normally distributed continuous variables and Chi^2-tests for categorical variables. For categorical variables with an expected count less than five, Fisher's exact tests were used. In the main analysis, the dependent variable was SCP receipt as reported by the patient. In additional analyses, dependent variables were generated SCPs, reported receipt of follow-up SCPs and generated follow-up SCPs. Independent variables were patient- or provider -level factors. Independent variables with a significance level greater than 0.05 were entered into a multivariable logistic regression model using a forward selection method. For each selected independent variable, the odds of SCP receipt as reported by the patient was estimated (SCP received versus no SCP received). A significance level of 0.05 was used.

RESULTS

SCP receipt

Of all 178 patients in the intervention arm of the trial, an SCP was *generated* for 90% of the patients (N=161). From the patients for whom an SCP was *generated*, 70% (N=125) *reported* receipt of an SCP (figure 1).

Patient and SCP care provider factors related to SCP receipt

In univariate analysis, patients who *reported* first SCP receipt were significantly younger (65 years versus 70 years, p<0.01) and less often had Type D personality (15% vs. 31%, p=0.02) compared to patients that *reported* no first SCP receipt (table 1). In endometrial cancer patients, first SCPs were more often received by patients with an advanced FIGO stage (table 1). No SCP care provider factors were associated with first SCP receipt (table 2).

Multivariate analysis showed that older age, having ovarian cancer vs endometrial cancer, having Type D personality versus no type D personality and completion of the questionnaire a shorter period of time after the SCP consult were all independently associated with a lower chance of *reported* first SCP receipt (table 3).

Reported receipt of follow-up SCPs was associated with hospital (p<0.01) and having an oncology nurse as SCP provider compared to a gynecologist/oncologic gynecologists (31% vs. 10%, p<0.01) (not tabulated). No patient factors were associated with receipt of follow-up SCPs. Follow-up SCPs were *reported* as received by 21% (N=27) of the patients (data not shown).

Additional analyses showed that first SCPs were more often *generated* for endometrial compared to ovarian cancer patients (95% vs. 82%, p<0.01). Follow-up SCPs were also more often *generated* for endometrial compared to ovarian cancer patients (24% vs. 11%, p=0.04) and more often for ovarian cancer patients who had surgery only compared to ovarian cancer patients who also had chemotherapy (40% vs. 9%, p=0.04) (not tabulated).

In addition, 36 patients (20%) for whom a first SCP was generated (N_{total}=161) did not report receiving an SCP. These patients were significantly older compared to patients who *reported* first SCP receipt (71 [SD 8.0] versus 65 [SD 10], p<0.01) (not tabulated).

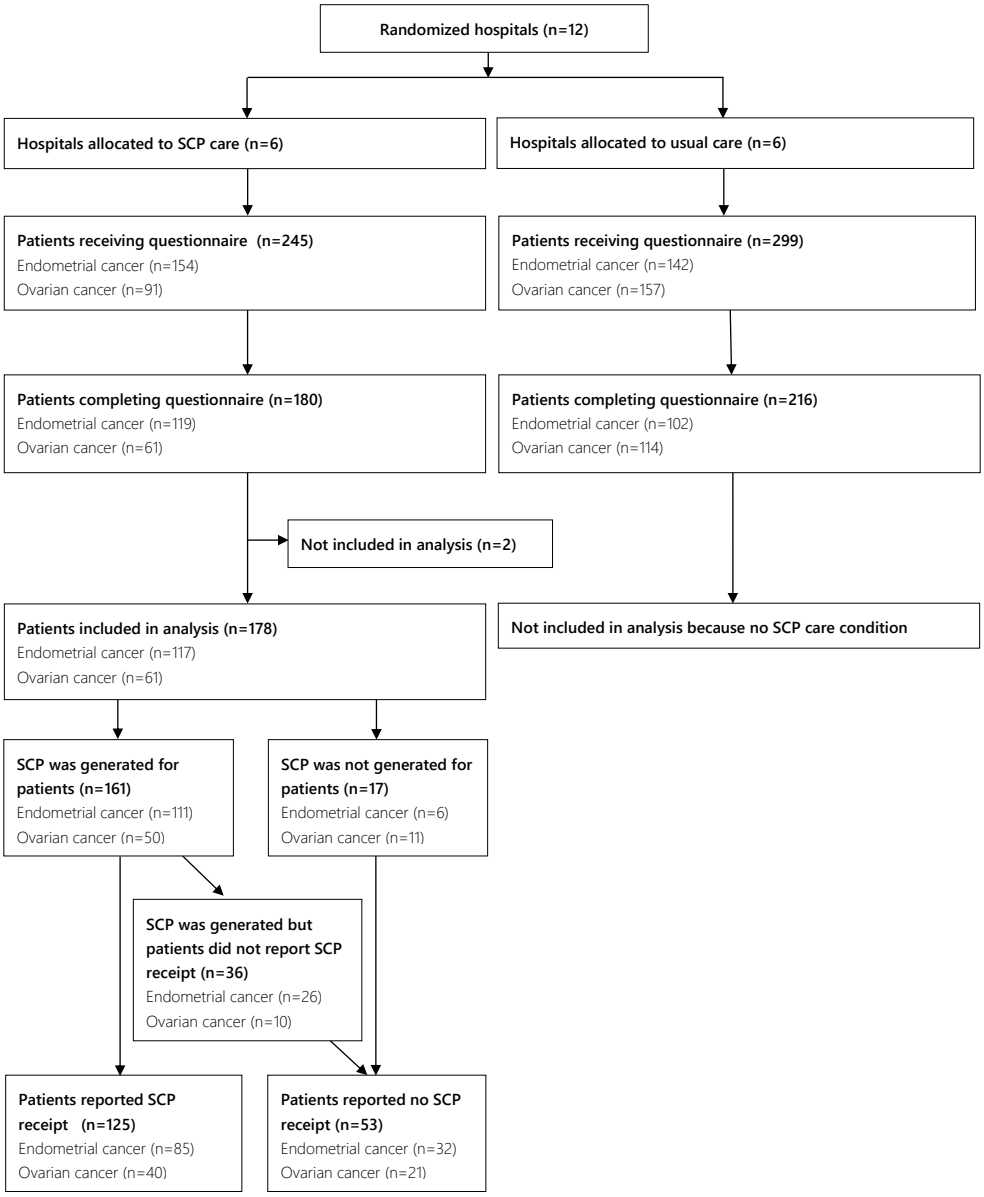

Figure 1: Flow diagram of patients included in analysis and (first) SCP receipt in the ROGY care trial

Table 1: patient factors of reporting first SCP receipt

	SCP Received (N=125)	SCP Not received (N=53)	P-value
Age, mean (SD)	64.7 (10.2)	70.4 (8.6)	**<0.01**
Cancer type, N (%)			
endometrial	85 (68)	32 (60)	0.33
ovarian	40 (32)	21 (40)	
Endometrial cancer			
FIGO stage, N (%)			
I	68 (80)	32 (100)	0.051
II	6 (7)	0 (0)	
III	9 (11)	0 (0)	
IV	2 (2)	0 (0)	
Treatment type			
Surgery only	53 (64)	16 (50)	0.07
Radiotherapy	25 (30)	16 (50)	
Chemotherapy	5 (6)	0 (0)	
Ovarian cancer			
FIGO stage, N (%)			
I	15 (38)	6 (28)	0.43
II	6 (15)	1 (5)	
III	14 (35)	9 (43)	
IV	5 (12)	5 (24)	
Treatment type			
Surgery only	10 (26)	5 (25)	0.96
Chemotherapy	29 (74)	15 (75)	
SES, N (%)			
low	20 (18)	12 (25)	0.14
medium	41 (36)	21 (45)	
high	53 (47)	14 (30)	
Partner			
Yes	93 (76)	38 (73)	0.66
No	29 (24)	14 (27)	
Health literacy[a], N(%)			
low	38 (45)	7 (28)	0.15
medium	40 (47)	13 (52)	
high	7 (8)	5 (20)	
Type D personality, N (%)			
yes	18 (15)	15 (31)	**0.02**
no	105 (85)	34 (69)	
Comorbidities, N (%)			
0	17 (14)	4 (8)	0.09
1	32 (26)	21 (43)	
>1	75 (60)	24 (49)	
Weeks between SCP consult and questionnaire, median(25^{th}-75^{th})	10.7 (7.0-14.6)	11.2 (7.0-15.9)	0.43

[a] Low = being somewhat, a little or not at all confident filling out medical forms; medium = being quite confident filling out medical forms; high = being very confident filling out medical forms. Health literacy was unknown for n=68.Note [1]P-values are based on independent samples t-tests for continuous variables and Chi^2-tests/ Fisher's exact tests for categorical variables. [2]All percentages stated are column percentages.

Table 2: SCP provider factors of reporting first SCP receipt

	SCP received (N=125)	SCP not received (N=53)	P-value
Hospital, N (%)			
1	27(22)	10 (19)	
2	14(11)	6 (11)	
3	23 (18)	10 (19)	
4	36 (29)	17 (32)	
5	10 (8)	4 (8)	
6	15 (12)	6 (11)	0.98
SCP Care provider, N (%)			
Gynecologist/ OG	63 (50)	27 (51)	
Oncology Nurse	62 (50)	26 (49)	1.00
Age SCP provider, Mean (SD)	43.5 (5.0)	43.2 (5.2)	0.75
Gender SCP provider, N (%)			
Male	9 (7)	4 (8)	
Female	116 (93)	48 (92)	1.00
Motivation regarding SCP provision, mean (SD)			
Range 0-10	8.1 (0.7)	8.0 (0.7)	0.94
Opinion about SCP benefit, mean (SD)			
range 0-10	7.4 (1.1)	7.4 (1.1)	0.90

Note [1]P-values are based on independent samples t-tests for continuous variables and Chi^2-tests/ Fisher's exact tests for categorical variables.

Table 3: odds ratio's (OR) of first SCP receipt versus no first SCP receipt

	SCP received versus not received (N=146)		
	OR	95% CI	P-value
Age, per 10 years	0.35	0.20-0.57	**<0.01**
Cancer type,			
Endometrial	1.00 (ref)		
Ovarian	0.31	0.12-0.83	**0.02**
Type D personality,			
Yes	0.28		
No	1.00 (ref)	0.11-0.73	**<0.01**
Comorbidities			
0	1.00 (ref)		
1	0.37	0.07-1.65	0.22
>1	1.12	0.21-4.82	0.89
Time between SCP consult and questionnaire, per week	0.95	0.90-1.00	**0.04**

Note: Candidate variables for multivariate regression were all patient factors (age, cancer type, FIGO stage, treatment type, socio-economic status, health literacy, Type D personality, number of comorbidities and number of weeks between SCP consult and questionnaire) and SCP Care provider factors (hospital, SCP Care provider, age, gender, motivation regarding SCP provision and opinion about SCP benefit). Candidate variables with a significance level higher than 0.05 were entered into a multivariate regression model using a forward selection method. Selected variables were entered into a separate multivariate regression model in order to include all patients in the model for whom data was available on selected variables.

DISCUSSION

In this study of endometrial and ovarian cancer survivors in the intervention arm of the ROGY care trial, first SCPs were generated for 90% of the patients and reported as received by 70% of the patients. Follow-up SCPs were reported as received by 21% of the patients. Patient factors, including being older, having ovarian cancer and having a Type D personality were independently associated with a lower chance of perceived receipt of first SCPs, while having an oncology nurse as care provider was associated with higher perceived receipt of follow-up SCPs.

To our knowledge, this is the first study that examines patient and care provider factors associated with SCP receipt in a trial. The self-reported SCP receipt in our trial is substantially higher compared to the coverage ranging between 24% and 58% in observational studies.[35] This is probably related to the ease with which the SCP could be automatically generated through ROGY by clicking a button. However, due to the pragmatic nature of the trial, 100 percent dissemination of SCP receipt was not attained.

Interestingly, we found that a considerable group of patients reported no SCP receipt while an SCP was generated. These patients were older on average compared to patients who did report receiving an SCP. There are two possible explanations for this finding: SCP receipt may have been underreported by older patients due to a recall bias; or during consultation SCP care providers decided more often not to hand over the SCP to older patients. In line with our findings, younger age has previously been associated with higher self-reported SCP receipt in observational studies.[20,21] This has formerly been explained by a higher need for instructions for follow-up care in younger cancer patients.[20] In addition, recall bias may explain lower self-reported SCP receipt in older patients.

Cancer type has also previously been associated with differences in SCP receipt. In two observational studies, patients with more common types of cancer, including breast-, prostate-, lung- and colorectal- cancer reported SCP receipt more often compared to patients with less common types of cancer such as melanoma and gynecological cancers.[20,21] It is possible that this is related to the fact that SCP templates are less available for less common types of cancer.[3,36] SCP receipt in endometrial and ovarian cancer patients specifically has not previously been investigated. Brothers and coworkers' SCP trial in gynecological cancer patients did not examine how many SCPs were actually received in the intervention arm.[9] Our study showed that SCPs were more often generated for, and more often reported as received by, endometrial cancer patients compared to ovarian cancer patients. Maybe, SCP care providers perceive more barriers to providing information to cancer patients with worse prognosis. This is in accordance with literature showing that health care providers are often reluctant to provide information on late

effects in order to prevent disproportionate fear in the patient.[37] Further, ovarian cancer patients less often received follow-up SCPs when they had chemotherapy compared to surgery only. This could be explained by the fact that during chemotherapy, treatment of the patient is scheduled for follow-up visits at the medical oncologist instead of the gynecologist/oncologic gynecologist.[25] Medical oncologists were not involved in our trial and therefore did not provide SCPs.

Besides younger age and cancer type, other studies found that higher SES is associated with higher perceived SCP receipt.[20,21] In addition, higher health literacy has been associated with higher perceived information provision.[38] Although we did not find statistically significant differences, our data suggest positive trends between SES and perceived SCP receipt, and health literacy and perceived SCP receipt.

To date, no patient personality factors have been studied in relation to SCP receipt. Our study shows that patients with a Type D personality (a combination of negative affect and social inhibition), were more likely to report no SCP receipt. Patients with this personality type have the tendency to experience increased negative emotions and tend not to share these emotions because of fear of rejection or disapproval.[33] In this study, 19% of the patients had a Type D personality, which is comparable to 21% in the general population.[33] Other studies have shown that cancer patients with a Type D personality are less likely to report receipt of both oral and written information.[32] SCP receipt in patients with a Type D personality may have been underreported. This may be due to negative emotions they experience towards medical information,[32] or because SCP care providers may be more reluctant to provide SCPs for patients that are more inhibited and less likely to ask for information. Future research should explore whether information needs are lower among patients with a Type D personality and consequently whether lower provision of SCPs for patients with a Type D personality is desired.

A minority of the patients in our study received a follow-up SCP. We found that follow-up SCP receipt, but not first SCP receipt, was higher in hospitals where SCP care was delegated to an oncology nurse. This was mainly due to the presence of one oncology nurse that provided SCP care for a large number of the patients in our analysis. Therefore, the generalizability of this finding is questionable. Moreover, we could not adjust for the patients' need of an updated SCP (i.e. when there were changes in the cancer, treatment, or care provider), which could have biased our results. However, previous studies also suggest that oncology nurses promote successful implementation of SCPs.[18,39] Consistently, prior results from the ROGY care trial showed that oncology providers in our study (i.e. gynecologists, gynecologic oncologists and oncology nurses) prefer oncology nurses to provide SCPs in their practice.[25] Therefore, for improved implementation of follow-up SCPs, delegation of SCP care to an oncology nurse is recommended. However,

oncology nurses did not provide first SCPs more often compared to gynecologists/ oncologic gynecologists in our study. Another suggestion to improve implementation of follow-up SCPs may be that the follow-up SCPs' content is tailored to the information needs of the patient during follow-up. In our trial, follow-up SCPs only differed from first SCPs when there were substantial differences in the treatment or care provider. If other information is provided in a follow-up SCP than the first SCP, care providers would probably be more prone to provide follow-up SCPs. Further, it would probably be helpful for the care provider if a reminder is sent when a follow-up SCP needs to be delivered.

A strength of the current study is the trial design, in which a large number of patient- and SCP care provider factors were measured along with longitudinal objective and subjective measures of SCP receipt. In addition to self-reported receipt of SCPs that has been examined in previous literature, we were able to examine whether an SCP was generated or not. This revealed new insights into, for instance, a possible recall bias of reported SCP receipt related to older age, and more certainty about factors influencing actual SCP receipt including cancer type and Type D personality.

In order to maximize the generalizability of our trial results, the ROGY care trial is characterized by a pragmatic approach; exclusion criteria for patient inclusion were limited and oncology providers were free to choose how the SCP provision was integrated in clinical practice. Despite the pragmatic nature of the trial, however, adherence to SCP provision by the care providers was probably higher than we would expect in clinical practice outside a trial setting.[3,36] For instance, SCP care providers in our trial frequently received reminders for patient inclusion and providing an SCP if not done so yet. This is reflected by a relatively long period between SCP provision and completion of the questionnaire by the patient. Our findings may therefore not be fully generalizable to everyday routine clinical practice.

Limitations of our study include the uncertainty of our measure of SCP receipt; although we were able to objectively examine whether an SCP was generated through ROGY, we are not sure whether the SCP was handed over to the patient. Therefore, we have to rely on self-report of the patient. However, our results suggest that the self-reported assessment of SCP receipt may have been affected by recall bias in older patients. Besides that, independent from age, patients who completed the questionnaire a longer period of time after the SCP consult were more likely to report no SCP receipt. A delay in completion of the questionnaire was either caused by a longer time needed for the gynecologist to include a patient in the study and sending the questionnaire, or by the patient taking a longer time before filling out the questionnaire after receiving the questionnaire. Either way, this may indicate a recall bias of self-reported SCP receipt. Future studies should therefore aim to include a more reliable measure of SCP receipt in the study, for instance

by sending a questionnaire shortly after SCP receipt in order to prevent recall bias. Alternatively, SCP receipt could be recorded by the care provider, but this may result in over-report of SCP receipt due to a social desirability bias.

The level of implementation fidelity of SCPs in the ROGY care trial is expected to have an influence on the observed effectiveness of SCPs. When no 100 percent coverage of SCP receipt in the intervention arm is attained, a comparison between the intervention and control arm (intention to treat analysis) may result in an underestimation of SCP effectiveness on patient reported outcomes. Therefore, a per protocol analysis could provide a more accurate estimation, by only comparing patients who reported SCP receipt to all patients in the usual care arm.[7] The current study shows, however, that SCP receipt may have been underreported due to recall bias. Subsequently, only patients who accurately remembered SCP receipt (i.e. because of younger age or more extensive discussion of SCP by the care provider) were included, which may result in an overestimation of SCP effectiveness. Therefore, both types of analysis require careful interpretation. It remains debatable whether a per protocol analysis based on actually generated SCPs instead of self-reported SCP receipt would better reflect SCPs effectiveness in the ROGY care trial.

Our findings can support future implementation of SCPs in clinical practice if widespread implementation is decided upon, or future clinical trial research. Disparities in SCP care could be reduced by paying particular attention to older patients and patients with ovarian cancer, who appear to less often receive SCPs. In addition, SCP care providers should pay particular attention to patients with a Type D personality, as they experience more negative emotions towards medical information and are not likely to ask for information themselves. However, the question arises whether all patients are in need of information as provided in an SCP. For instance, whether patients with a distressed personality benefit from SCP receipt instead of unnecessarily accumulating psychosocial distress, requires further investigation.[7] Possibly, more personalized SCPs (i.e. modules fitting individual patients' information needs) could promote information provision for cancer survivors in clinical practice.

REFERENCES

1. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
2. Health Council of the Netherlands. *Follow-up in oncology. Identify objectives, substantiate actions*. The Hague: Health Council of the Netherlands;2007.
3. Birken SA, Mayer DK, Weiner BJ. Survivorship care plans: prevalence and barriers to use. *Journal of cancer education : the official journal of the American Association for Cancer Education.* Jun 2013;28(2):290-296.
4. Schootman M, Homan S, Weaver KE, Jeffe DB, Yun S. Peer Reviewed: The Health and Welfare of Rural and Urban Cancer Survivors in Missouri. *Preventing chronic disease.* 2013;10.
5. Casillas J, Syrjala KL, Ganz PA, et al. How confident are young adult cancer survivors in managing their survivorship care? A report from the LIVESTRONG Survivorship Center of Excellence Network. *Journal of cancer survivorship : research and practice.* Dec 2011;5(4):371-381.
6. Rechis R, Beckjord EB, Nutt S. Potential benefits of treatment summaries for survivors' health and information needs: results from a LIVESTRONG survey. *Journal of oncology practice / American Society of Clinical Oncology.* Jan 2014;10(1):75-78.
7. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
8. Mayer DK, Birken SA, Chen RC. Avoiding Implementation Errors in Cancer Survivorship Care Plan Effectiveness Studies. *Journal of Clinical Oncology.* 2015:JCO. 2015.2062. 6937.
9. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
10. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
11. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment.* 2013;138(3):795-806.
12. Parry C, Kent EE, Forsythe LP, Alfano CM, Rowland JH. Can't see the forest for the care plan: a call to revisit the context of care planning. *Journal of Clinical Oncology.* 2013;31(21):2651-2653.
13. Carroll C, Patterson M, Wood S, Booth A, Rick J, Balain S. A conceptual framework for implementation fidelity. *Implementation science : IS.* 2007;2(1):40.
14. Stricker CT, Jacobs LA, Risendal B, et al. Survivorship care planning after the institute of medicine recommendations: how are we faring? *Journal of cancer survivorship : research and practice.* Dec 2011;5(4):358-370.
15. Dulko D, Pace CM, Dittus KL, et al. Barriers and facilitators to implementing cancer survivorship care plans. *Oncology nursing forum.* Nov 2013;40(6):575-580.
16. Chubak J, Tuzzio L, Hsu C, et al. Providing care for cancer survivors in integrated health care delivery systems: practices, challenges, and research opportunities. *Journal of oncology practice / American Society of Clinical Oncology.* May 2012;8(3):184-189.
17. Merport A, Lemon SC, Nyambose J, Prout MN. The use of cancer treatment summaries and care plans among Massachusetts physicians. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer.* Jul 2012;20(7):1579-1583.
18. Hewitt ME, Bamundo A, Day R, Harvey C. Perspectives on post-treatment cancer care: qualitative research with survivors, nurses, and physicians. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jun 1 2007;25(16):2270-2273.
19. Faul LA, Luta G, Sheppard V, et al. Associations among survivorship care plans, experiences of survivorship care, and functioning in older breast cancer survivors: CALGB/Alliance 369901. *Journal of cancer survivorship : research and practice.* Dec 2014;8(4):627-637.

20. Jabson JM, Bowen DJ. Cancer treatment summaries and follow-up care instructions: which cancer survivors receive them? *Cancer causes & control : CCC.* May 2013;24(5):861-871.
21. Sabatino SA, Thompson TD, Smith JL, et al. Receipt of cancer treatment summaries and follow-up instructions among adult cancer survivors: results from a national survey. *Journal of cancer survivorship : research and practice.* Mar 2013;7(1):32-43.
22. van de Poll-Franse LV, Nicolaije KAH, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2011;12:256.
23. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *Eur J Cancer.* 2011;47(14):2188-2194.
24. Zwarenstein M, Treweek S, Gagnier JJ, et al. Improving the reporting of pragmatic trials: An extension of the CONSORT statement. *BMJ* 2008;337:a2390.
25. Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, van de Poll-Franse LV, Kruitwagen RF. Oncology providers' evaluation of the use of an automatically generated cancer survivorship care plan: longitudinal results from the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Jun 2014;8(2):248-259.
26. Ezendam NP, Nicolaije KA, Kruitwagen RF, et al. Survivorship Care Plans to inform the primary care physician: results from the ROGY care pragmatic cluster randomized controlled trial. *Journal of cancer survivorship : research and practice.* Dec 2014;8(4):595-602.
27. Hewitt M, Greenfield S, Stovall E, eds. *From cancer patient to cancer survivor: lost in transition.* Washington, DC: National Academies Press; 2006.
28. Ganz PA, Hahn EE. Implementing a survivorship care plan for patients with breast cancer. *J Clin Oncol* 2008;26:759-767.
29. Netherlands Cancer Registry (NCR). Netherlands Cancer Registration *URL: http://www.cijfersoverkanker.nl/ [accessed 30-01-2015]* 2015.
30. Van Duijn C, Keij I. Sociaal-economische status indicator op postcode niveau. *Maandstatistiek van de bevolking.* 2002;50(2):32-35.
31. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Care & Research.* 2003;49(2):156-163.
32. Husson O, Denollet J, Oerlemans S, Mols F. Satisfaction with information provision in cancer patients and the moderating effect of Type D personality. *Psycho-Oncology.* 2013;22(9):2124-2132.
33. Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. *Psychosomatic medicine.* 2005;67(1):89-97.
34. Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *health.* 2004;11:12.
35. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
36. Birken SA, Deal AM, Mayer DK, Weiner BJ. Determinants of survivorship care plan use in US cancer programs. *Journal of cancer education : the official journal of the American Association for Cancer Education.* Dec 2014;29(4):720-727.
37. Cox A, Faithfull S. 'They're survivors physically but we want them to survive mentally as well': health care professionals' views on providing potential late effect information. *Supportive Care in Cancer.* 2013;21(9):2491-2497.
38. Verkissen MN, Ezendam NP, Fransen MP, et al. The role of health literacy in perceived information provision and satisfaction among women with ovarian tumors: a study from the population-based PROFILES registry. *Patient education and counseling.* 2014;95(3):421-428.
39. Hahn EE, Ganz PA. Survivorship programs and care plans in practice: variations on a theme. *Journal of Oncology Practice.* 2011;7(2):70-75.

Chapter 3

Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up – the ROGY Care trial

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ABSTRACT

Objective: The aim of this study was to assess the long-term impact of an automatically generated Survivorship Care Plan (SCP) on patient reported outcomes in ovarian cancer in routine clinical practice. Outcome measures included satisfaction with information provision and care, illness perceptions and health care utilization.

Methods: In this pragmatic cluster randomized trial, twelve hospitals in the South of the Netherlands were randomized to 'SCP care' or 'usual care'. All newly diagnosed ovarian cancer patients in the 'SCP care' arm received an SCP that was automatically generated by the oncology provider, by clicking a button in the web-based Registrationsystem Oncological GYnecology (ROGY). Ovarian cancer patients (N=174, mean age 63.3, SD=11.4; all stages) completed questionnaires directly after initial treatment and after 6, 12 and 24 months.

Results: First questionnaires were returned from 61 (67%) ovarian cancer patients in the 'SCP care' arm and 113 (72%) patients in the 'usual care' arm. In the 'SCP care' arm, 66% (N=41) of the patients reported receipt of an SCP. No overall differences were observed between the trial arms on satisfaction with information provision, satisfaction with care or health care utilization. Regarding illness perceptions, patients in the 'SCP care' arm had lower beliefs that the treatment would help to cure their disease (overall, 6.7 vs. 7.5, $p<0.01$).

Conclusions: SCPs did not increase satisfaction with information provision or care in ovarian cancer patients. Our trial results suggest that patients may not benefit from an SCP.

INTRODUCTION

The number of cancer patients that live with or beyond cancer is increasing worldwide, due to earlier detection, rapid improvement of treatments and ageing.[1] Consequently, a growing number of cancer survivors face physical and psychological challenges in life after treatment.[2] The provision of Survivorship Care Plans (SCPs), yielding patient-tailored information for cancer survivors to deal with these challenges, has been widely recommended for all cancer survivors.[3] However, evidence for informed implementation of SCPs in routine clinical practice is limited.[4,5]

Three randomized controlled trials (RCTs) did not find an effect of SCPs on short or long-term satisfaction with care, quality of life or distress.[6-9] The ROGY care trial was the first RCT with a pragmatic cluster randomized design, which maximizes external validity and prevents contamination between trial arms.[10] Prior results from the ROGY care trial showed that in endometrial cancer patients, automatically generated SCPs increased the perceived amount of information received but did not improve satisfaction with information provision or care, up to one year after diagnosis.[11] In contrast to the other RCTs, the ROGY care trial found an effect on other outcomes: SCPs increased worry, emotional impact, experienced symptoms and contact with the primary care physician about their disease.[11] Based on current evidence, no definite conclusions can be drawn on the benefit of SCPs. Moreover, potential negative consequences should be considered. The ROGY care trial was designed and powered to separately evaluate the impact of SCPs in endometrial and ovarian cancer patients in order to take into account the potential moderation effect of different treatment regimens and prognosis between these two types of cancer.

In contrast to endometrial cancer, ovarian cancer is often detected at an advanced stage, resulting in a poor prognosis.[12] Current 5-year survival of ovarian cancer patients is only 38-46% in developed countries.[12,13] Subsequently, information provided in an SCP (i.e. patients' cancer stage and grade, patients' treatments and long-term and late effects of the treatments) is often unfavorable and may be perceived as threatening. The initial hypotheses of the ROGY care trial was that SCPs would have a positive effect on patient reported outcomes. However, earlier findings from the ROGY care trial related to patients with endometrial cancer suggest that SCPs may also increase threatening illness perceptions. We now expect that SCPs worsen illness perceptions in ovarian cancer patients likewise the outcomes in endometrial cancer patients.

The current study aims to assess the impact of automatically generated SCPs in the ROGY care trial on patient-reported outcomes in ovarian cancer patients up to two years after diagnosis, including satisfaction with information provision and care, illness perceptions and health care utilization.

METHODS

Design

The pragmatic cluster randomized ROGY care trial among 221 endometrial and 174 ovarian cancer patients was conducted to assess the longitudinal impact of automatically generated SCPs on patient and health care provider reported outcomes. In the south of the Netherlands, twelve hospitals were randomly allocated to either 'usual care' or 'SCP care'. The trial was centrally approved by a Medical Research Ethics Committee, as well as by each participating center.[10] Accordingly, the current study describes the results of the impact of SCPs on patient reported outcomes in ovarian cancer patients. The impact of SCPs on health care provider reported outcomes has been described previously.[14]

Participants and recruitment

All patients newly diagnosed with ovarian cancer as a primary tumor between April 2011 and March 2014 were invited to participate. Patients were excluded if they had borderline ovarian cancer, were undergoing palliative care or were unable to complete a Dutch questionnaire.[10] All eligible patients in both trial arms were included in the study shortly after initial treatment. Patients were invited to take part by means of a letter, accompanied with an informed consent form and a questionnaire, provided to the patient by their own gynecologist.[10,15] After consent, follow-up questionnaires were sent directly to the patients' home address at 6, 12, 18 and 24 months after treatment (Figure 1). Questionnaires collected at 18 months after diagnosis did not include questions on any of the outcomes in the current study and was therefore not included in the current analysis.

Randomization and blinding

To avoid potential contamination between the trial arms, a cluster-randomized design with randomization on hospital-level was chosen. Hospitals were included if they used the registration system ROGY, which was needed to generate SCPs. To prevent imbalance between the trial arms, stratified randomization was used according to whether a hospital has a Gynecologic Oncology Center, and the annual number of endometrial and ovarian cancer patients diagnosed in each hospital. Randomization was performed via a table of random numbers, by an independent researcher blinded to the identity of the hospitals. Patients, but not oncology providers or researchers assessing the outcomes, were blinded to trial assignment.[16]

SCP care versus usual care

In the hospitals that were allocated to 'usual care', standard care was provided in accordance to the Dutch follow-up guidelines. These guidelines include: verbal and written information about the period after treatment and follow-up, about signs of recurrence, and hospital contact details. In most hospitals, verbal information and the

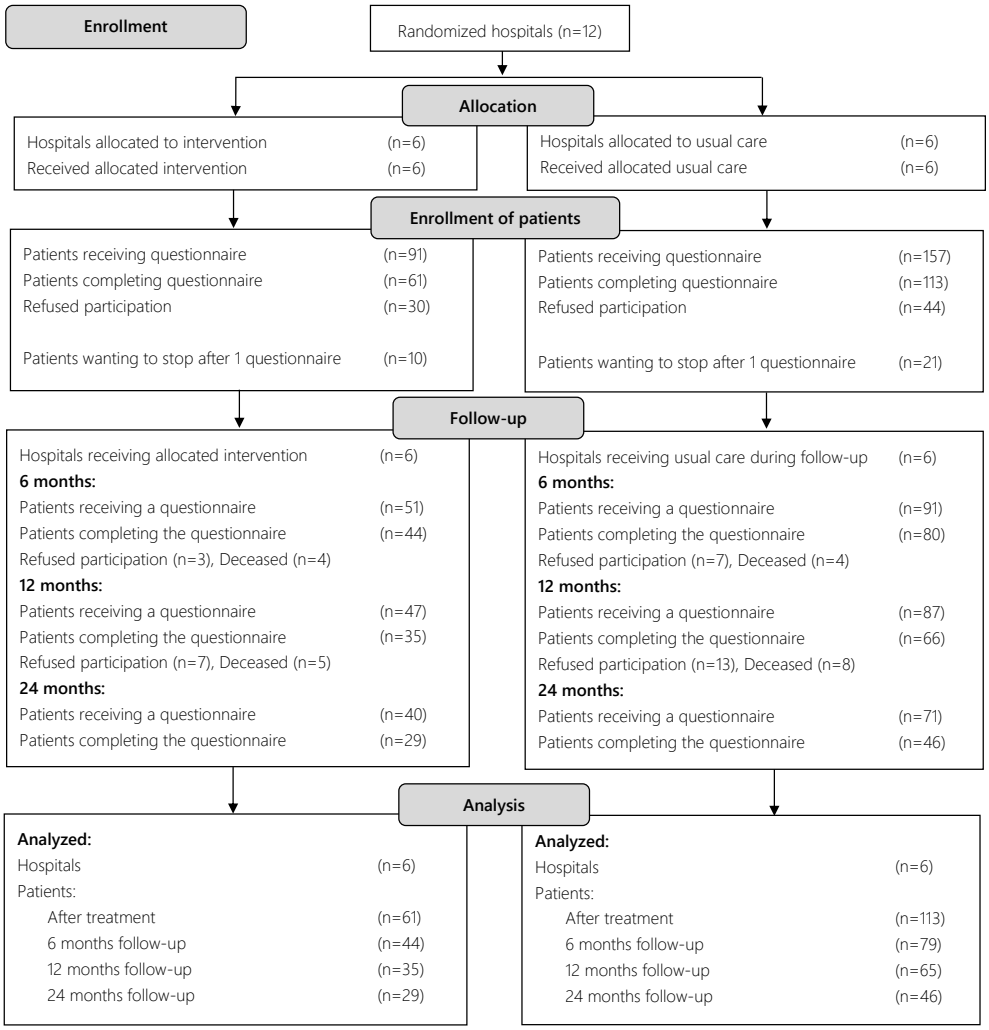

Figure 1: CONSORT Flow diagram of ovarian cancer patient enrollment

generic brochures of the Dutch Cancer Society were provided.[17] None of the hospitals provided SCPs as developed for this study.

In the hospitals that were allocated to 'SCP care', all oncology providers (gynecologist/gynecologic oncologist and oncology nurses, N=24) attended an instruction evening devoted to when and how SCPs should be provided. They were instructed to provide an SCP to patients at the consultation where the results of histopathology and (adjuvant) treatment plan were discussed, mostly 7-14 days after surgery. If applicable (i.e. if there were any changes in the cancer, treatment or oncology provider), an updated version of the SCP could optionally be discussed in a follow-up consultation.[18] In addition,

care providers were instructed to send a copy of the SCP to the patient's primary care physician.[19] In the Netherlands, follow-up care is provided by an oncology provider up to 5 years after diagnosis (www.oncoline.nl). Therefore, the SCP was not meant to transition the patient from oncology care to primary care, but to inform the patient about the treatments, long-term and late effects of the treatments and support services. Practical guidelines were given on the components of the SCP that should minimally be discussed with each patient during the consultation (i.e. diagnosis, prognosis, treatment(s), most important side-effects). Because of the pragmatic approach of the trial, care providers in the 'SCP care' arm were free to choose whether the gynecologist/gynecologic oncologist, or oncology nurse provided the SCP fitting their clinical practice.[10]

Survivorship care plan

The SCP was based on the Dutch translation of the American Institute of Medicine (IOM) SCP template,[20] adjusted to the local situation[21] by a group of gynecologists/gynecologic oncologists, oncology nurses, a radiotherapist, medical oncologist, primary care physician, and patients.[10] Texts of the SCP were based on pilot-tested patient education material from the Dutch Cancer Society. In addition, the SCP was pilot-tested on patients with a low/intermediate educational level to ensure that the SCP was understandable.

The SCP consisted of a tailored treatment summary including information on diagnostic tests, type of cancer, stage, grade and treatments received (type of treatment, date and medical specialist) and contact details of the hospital and medical specialists. The treatment summary contained explanatory notes of the clinical information provided and visual representations of affected organs and cancer stage of the patient. In addition, the SCP contained a tailored follow-up care plan, including detailed information on the most common short- and long-term effects of the treatments received, effects on social and sexual life, possible signs of recurrence and secondary tumors, and information on rehabilitation, psychosocial support, and supportive care services.[10] To make sure that patients were aware of receiving an SCP, the front page clearly stated "Survivorship Care Plan".

Measures

Age, socio-economic status (SES) and clinical data, such as cancer type, cancer stage and date of diagnosis, were obtained from the Netherlands Cancer Registry (NCR). The NCR routinely collects data on newly diagnosed cancer patients in all hospitals in the Netherlands.[22] SES was based on postal code of the residence area of the patient, combining aggregated individual fiscal data on the economic value of the home and household incomes.[23] SES was categorized into low, medium or high. Data obtained from the NCR were available for both participants and non-participants in the trial. Among the participants of the trial, additional socio-demographic information (i.e. marital status,

employment status and comorbidities) was assessed in the first questionnaire. Marital status ('married/living together' versus 'divorced/widowed/never married') and employment status ('having a paid job' versus 'not having a paid job') were dichotomized. Comorbidity was assessed by the adapted Self-administered Comorbidity Questionnaire (SCQ), and categorized into no comorbidities, one comorbidity or more than one comorbidities.[24]

Information provision was assessed with the EORTC-QLQINFO25.[25] Scales included four multi-item subscales (information about the disease, medical tests, treatment and other care services) and four single-item scales (information about different places of care, things you can do to help yourself get well, satisfaction with the information, helpfulness of the information). All scales indicated a score between 0 (low perceived information provision) and 100 (high perceived information provision). Internal consistency of the scales (Cronbach's alphas 0.75-0.90) were good. Test-retest reliability (intraclass correlations 0.71-0.91) were good.[25]

Satisfaction with care was assessed with the EORTC INPATSAT32.[26] Scales included two multi-item scales (doctor's interpersonal skills and nurses' interpersonal skills) and two singe-items scales (exchange of information between caregivers and general satisfaction with care). All scales indicated a score between 0 (low perceived quality of care) and 100 (high perceived quality of care). Internal consistency of the scales (Cronbach's alphas 0.93-0.94) were good. Test-retest reliability (intraclass correlations 0.66-0.85) were good.[26]

Illness perception was assessed with the Brief Illness Perception Questionnaire (B-IPQ).[27] Scales included eight single-time scales regarding cognitive illness representations (how much illness affects life, how long illness will continue, how much patient has control over illness, how much treatment helps to cure illness, how many symptoms are experienced), emotional representations (how concerned patient is about illness, how much patient is affected emotionally) and comprehensiveness (how well patient understands illness). All scales indicated a score between 0 (low endorsement) and 10 (high endorsement). Test-retest reliability (Pearson correlations 0.42-0.75) was good.[27]

Health care utilization was assessed by the number of visits that were made to a medical specialist or primary care physician in relation to cancer in the past 6 months.

Actual receipt of an SCP was assessed in the first questionnaire ("Did you receive a Survivorship Care Plan?"), in both trial arms. In addition, patients were asked how many times they received the SCP at 6, 12 and 24 months after treatment. If patients in the 'SCP care' arm reported SCP receipt but no SCP was generated in ROGY, they were not included in the per-protocol analysis because it was not possible to receive an SCP when not generated.

Statistical Analysis

Statistical analyses were conducted using Statistical Analysis System (SAS) version 9.4. (SAS Institute, Cary, NC, 1999). Differences in characteristics of patients between the trial arms, between participants and non-participants of the trial, and between participants that completed participation and participants lost to follow-up were compared using t-tests for normally distributed continuous variables, Mann-Whitney U-tests for not-normally distributed variables and chi-square tests for categorical variables.

Linear multilevel regression analysis was performed to assess the effect of SCPs on patient reported outcomes, allowing for adjustment of inter-dependency between repeated measures within patients[28] and correction for data missing at random.[29,30] A random intercept on the patient-level was included in the model to adjust for the inter-dependency between repeated measures. Based on likelihood ratio tests, neither a random intercept on the hospital-level (ICCs<0.16) to account for the cluster-design, nor a random-slope on the patient-level (ICCs<0.14) to account for potential dependency between the intervention and outcome variable, improved the model for any of the outcome variables and were therefore not included in the model. All a priori-selected covariates were entered into the model (i.e. age, time since diagnosis, marital status, socio-economic status, employment, comorbidities, stage, and treatment). Dependent variables were the information provision and care-, illness perceptions-, and health care utilization- scales. Additionally, we assessed whether the effect of SCPs differed for each time-point separately by adding a time-reference variable and an interaction term between trial arm and the time-reference variable to the overall model.[28]

Intention-to-treat analysis (ITT) compared all patients in the 'SCP care' (N=61) arm to all patients in the 'usual care' arm (N=113). Per-protocol (PP) analysis compared patients in the 'SCP care' arm who reported having received an SCP at any time during follow-up and where an SCP had been generated (N=40), to all patients in the usual care arm (N=113).

The ROGY care trial was powered to detect a clinically meaningful difference of 0.5 SD for SCP care versus usual care on the overall primary outcomes (satisfaction with information provision and satisfaction with care). A total of 150 patients were targeted (75 per trial arm) to attain 80% power, assuming an intra-class correlation (ICC) between the hospitals of 0.005.[10]

RESULTS

No differences were observed in socio-demographic or clinical baseline characteristics between the trial arms (Table 1) or between participants and non-participants of the trial

(Table 2). However, patients that were lost to follow-up during the trial had a significantly higher FIGO-stage (patients with stage IV, 25% vs. 8%, p=0.03) (Table 2).

Questionnaires were sent to 91 patients in the SCP care arm and 157 patients in the usual care arm. Questionnaires were returned after treatment by 61 patients (67%) in the SCP care arm and 113 patients (72%) in the usual care arm. Follow-up questionnaires were received after 6 months (48% SCP care; 51% usual care), 12 months (38% SCP care; 42% usual care) and 24 months (32% SCP care; 29% usual care) (Figure 1). Post-hoc power analysis show that for detecting a clinically meaningful difference of 0.5 SD on the outcomes, statistical power was sufficient for overall ITT analysis (96%) and for separate ITT analysis after diagnosis (88%), but lower for separate ITT analysis after 6 (75%), 18 (66%) and 24 (55%) months. For PP analysis, statistical power was sufficient for overall analysis of all time-points (89%), but low for analysis of separate time-points (77%, 63%, 52%, 44% respectively).

In the SCP care arm, 40 patients (66%) reported in the first questionnaire that they had received an SCP and 10 patients (16%) reported that they had received an updated follow-up SCP at 6, 12 or 24 months. In the usual care arm, 21 patients (18%) reported that they had received an SCP, and no patients reported receipt of an updated follow-up SCP.

Table 1: Baseline socio-demographic and clinical characteristics of participants according to trial arm

	Total participants (n=174)	SCP Care (n=61)	Usual Care (n=113)	P-value*
Patients				
Age at diagnosis				
Mean (SD)	63.3 (11.4)	63.3 (11.3)	63.3 (11.4)	0.97
Age at time of first questionnaire				
Mean (SD)	64.1 (10.8)	63.6 (11.2)	64.3 (10.7)	0.67
SES, n (%)				
Low	31 (18)	13 (21)	18 (16)	0.43
Intermediate	74 (42)	22 (36)	52 (46)	
High	70 (40)	26 (43)	44 (39)	
Months since diagnosis				
Median (IQR)	2.8 (1.6-4.1)	3.0 (1.8-4.2)	2.4 (1.6-4.1)	0.31
<1	34 (19)	8 (13)	26 (23)	0.15
1-2	57 (33)	18 (30)	39 (34)	
2-3	25 (14)	8 (13)	17 (15)	
>3	59 (34)	27 (44)	32 (28)	
Comorbidity[1]				
None	2 (2)	2 (4)	0 (0)	0.14
1	57 (33)	21 (34)	36 (32)	
2 or more	115 (66)	38 (62)	77 (68)	
Marital status[2]				
Partner	131 (75)	48 (79)	83 (73)	0.39
No partner	44 (25)	13 (21)	31 (27)	

Table 1: Continued

	Total participants (n=174)	SCP Care (n=61)	Usual Care (n=113)	P-value*
Employed				
Yes	51 (29)	20 (33)	31 (27)	0.44
No	124 (71)	41 (67)	83 (73)	
FIGO-stage, n (%)				
I	52 (30)	21 (34)	31 (28)	0.63
II	16 (9)	7 (11)	9 (8)	
III	74 (43)	23 (38)	51 (46)	
IV	30 (17)	10 (16)	20 (18)	
Treatment, n (%)				
Surgery	158 (91)	54 (88)	104 (93)	0.33
Chemotherapy	136 (79)	44 (72)	92 (82)	0.13
Hospital, n (%)				
1	16 (9)	16 (26)		
2	8 (5)	8 (13)		
3	5 (3)	5 (8)		
4	25 (14)	25 (41)		
5	3 (2)	3 (5)		
6	4 (2)	4 (7)		
7	37 (21)		37 (33)	
8	30 (17)		30 (26)	
9	25 (14)		25 (22)	
10	5 (3)		5 (4)	
11	4 (2)		4 (4)	
12	13 (7)		13 (11)	
Hospitals				
# endometrial and ovarian cancer patients per year				
≤50	4 (33)	2 (33)	2 (33)	
>50	8 (67)	4 (67)	4 (67)	
Gynecologic Oncology Center (Tertiary Referral Hospital)				
Yes	2 (17)	1 (17)	1 (17)	
No	10 (83)	5 (83)	5 (83)	

Note: *P-values report comparisons between the intervention arm and the usual care arm, according to t-tests, Wilcoxon-Mann-Whitney test and chi-square tests. Means (M) with standard deviations (SD) were used to describe normally distributed continuous variables, medians with interquartile range (IQR) to describe not-normally distributed continuous variables, and frequencies with percentages to describe categorical variables. [1]Comorbidities included heart disease, high blood pressure, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, blood disease, cancer, depression, pain and swelling in joints other than the back, osteoporosis and fractures.[2]Marital status included: partner = married/living together; no partner = divorced/widowed/never married. The numbers may not always add up to 100, because percentages have been rounded off to whole numbers.

Table 2: socio-demographic and clinical variables according to (non-)participation, complete participation and lost to follow-up

	Total participants (N=174)	Non-participants (N=74)	P-value	Complete participation (N=75)	Lost to follow-up (N=99)	P-value
Age at diagnosis						
Mean (SD)	63.3 (11.4)	65.1 (12.6)	0.27	62.2 (9.9)	64.2 (12.3)	0.25
Age at time of first questionnaire						
Mean (SD)	64.1 (10.8)	unknown		62.4 (9.9)	64.7 (12.0)	0.08
SES, n (%)						
Low	31 (18)	16 (23)	0.34	15 (22)	15 (16)	0.67
Intermediate	74 (42)	32 (46)		25 (37)	35 (38)	
High	70 (40)	21 (30)		28 (41)	41 (45)	
Marital status[1]						
Partner	131 (75)	unknown		57 (76)	74 (74)	0.76
No partner	44 (25)	unknown		18 (24)	26 (26)	
Employed						
Yes	51 (29)	unknown		22 (29)	29 (29)	0.96
No	124 (71)	unknown		53 (71)	71 (71)	
FIGO-stage, n (%)						
I	52 (30)	20 (28)	0.70	27 (36)	25 (26)	**0.03**
II	16 (9)	4 (5)		8 (11)	8 (8)	
III	74 (43)	35 (48)		34 (45)	40 (41)	
IV	30 (17)	14 (19)		6 (8)	24 (25)	
Treatment, n (%)						
Surgery	158 (91)	64 (88)	0.38	72 (96)	87 (89)	0.08
Chemotherapy	136 (79)	53 (73)	0.31	55 (73)	80 (81)	0.19
Comorbidity[2]						
None	2 (2)	unknown		19 (26)	30 (30)	0.82
1	57 (33)	unknown		21 (28)	27 (27)	
2 or more	115 (66)	unknown		34 (46)	43 (43)	
Hospital, n (%)						
1	16 (9)	2 (3)	0.33	16 (21)	21 (21)	0.69
2	8 (5)	3 (4)		9 (12)	7 (7)	
3	5 (3)	2 (3)		14 (19)	16 (16)	
4	25 (14)	15 (21)		11 (15)	14 (14)	
5	3 (2)	4 (5)		3 (4)	5 (5)	
6	4 (2)	4 (5)		4 (5)	1 (1)	
7	37 (21)	10 (14)		1 (1)	4 (4)	
8	30 (17)	12 (16)		10 (13)	15 (15)	
9	25 (14)	7 (10)		1 (1)	2 (2)	
10	5 (3)	3 (4)		1 (1)	3 (3)	
11	4 (2)	3 (4)		3 (4)	10 (10)	
12	13 (7)	8 (11)		2 (3)	2 (2)	

Note: P-values report comparisons between participants and non-participants, and between patients that completed participation and patients lost to follow-up, according to t-tests and Chi-square tests. Means (M) with standard deviations (SD) were used to describe normally distributed continuous variables and frequencies with percentages to describe categorical variables. Patients with complete participation completed baseline questionnaire and all follow-up questionnaires at 6, 12 and 24 months after diagnosis; patients lost to follow-up were patients that did not complete all follow-up questionnaires. [1]Marital status included: partner = married/living together; no partner = divorced/widowed/never married. . [2]Comorbidities included heart disease, high blood pressure, lung disease, diabetes, ulcer or stomach disease, kidney disease, liver disease, blood disease, cancer, depression, pain and swelling in joints other than the back, osteoporosis and fractures.The numbers may not always add up to 100, because percentages have been rounded off to whole numbers.

ITT analysis (N=174) showed no significant differences in satisfaction with information provision or satisfaction with care between patients in the SCP care arm and patients in the usual care arm overall. At 6 and 24 months after diagnosis, patients in the SCP care arm reported lower perceived information on other services (6 months: M=29.8, SD=23 vs. M=38.1, SD=25, P=0.02; 24 months: M=27.4, SD=23 vs. M=34.5, SD=20, P=0.03), but effect sizes were small (r=0.2). In the PP analysis (N=153), this difference remained only significant after 24 months (M=27.0, SD=23 vs. M=34.5, SD=20, P=0.048, r=0.2). Further, in ITT analysis only after 24 months, patients in the SCP care arm reported lower satisfaction with the interpersonal skills of the nurses (M=67.8, SD=22 vs. M=83.1, SD=14, P=0.04, r=0.4), but this difference was not significant in the PP analysis (M=63.3, SD=21 vs. M=83.1, SD=14, P=0.06, r=0.5) (Table 3).

In the ITT analysis overall, after diagnosis and after 6 and 12 months, patients in the SCP care arm reported lower beliefs that the treatment would help to cure the illness compared to patients in the usual care arm (overall: M=6.9, SE=0.2 vs. 7.5, SE=0.3, p<0.01, r=0.2; after diagnosis, M=7.2, SD=2.3; vs. M=7.8, SD=1.8, P=0.03, r=0.1; after 6 months, M=6.7, SD=2.9 vs. M=7.2, SD=2.4, P=0.04, r=0.1; after 12 months: M=6.4, SD=2.7 vs. M=7.2, SD=2.5, P<0.01, r=0.2) (Table 3, Figure 2). In PP analysis this finding was only significant overall (M=7.5, SE=0.2 vs. M=6.9, SE=0.3, P<0.01, r=0.2) and after 12 months (M=6.6, SD=2.6 vs. M=7.2, SD=2.5, P<0.01, r=0.1;Table 3).

In ITT analysis, patients in the 'SCP care' arm reported less visits to the medical specialist in the 6 months after treatment (M=4.9, SD=3.5 vs. M=7.6, SD=9.4, P=0.04, r=0.2 Table 3). In additional analysis, we also adjusted for time between first questionnaire and last treatment, to adjust for possible systematic differences in the timing of treatments between the hospitals which could explain the number of visits to the medical specialist, but results were similar (data not shown).

There were no interactions between trial arms and patients lost to follow-up for any of the outcomes, indicating that the effect of SCP care did not differ for patients who were lost to follow-up. There were also no interactions between the trial arms and time for any of the outcomes, indicating that the effect of SCP care did not differ over the time points.

Table 3: Effects of the intervention: overall, after diagnosis, and after 6, 12 and 24 months, for Intention to Treat analyses

	Overall	After diagnosis (N=174)			After 6 months (N=123)		
	Beta (95%CI)	M (SD) SCP care	M (SD) Usual care	Beta (95%CI)	M (SD) SCP care	M (SD) Usual care	Beta (95%CI)
INFORMATION PROVISION							
Disease	0.0 (-6.0; 6.0)	59.9 (19)	56.3 (24)	2.6 (-4.2; 9.4)	59.9 (22)	58.4 (20)	-0.8 (-8.5; 6.8)
Medical tests	-2.4 (-8.9; 4.1)	69.8 (23)	68.3 (24)	-0.5 (-7.9; 6.9)	69.6 (24)	71.0 (23)	-2.5 (-10.8; 5.8)
Treatment	-1.8 (-7.8; 4.2)	55.4 (24)	52.5 (22)	2.0 (-4.8; 8.9)	50.7 (28)	57.7 (22)	-7.2 (-15.0; 0.5)
Other services	-5.5 (-12.3; 1.3)	32.3 (23)	31.5 (24)	-0.6 (-8.4; 7.2)	29.8 (23)	38.1 (25)	**-10.9* (-19.7; -2.0)**
Places to go	1.6 (-6.7; 9.8)	32.2 (32)	28.2 (30)	1.8 (-8.5; 12.0)	26.8 (29)	24.4 (30)	-1.3 (-13.0; 10.4)
Things to do	-0.7 (-8.9; 7.5)	49.7 (32)	39.8 (34)	8.7 (-1.4; 18.7)	37.3 (31)	39.7 (31)	-3.1 (-5.9; 12.0)
Satisfaction	1.8 (-5.0; 8.7)	74.7 (22)	72.2 (26)	2.3 (-5.6; 10.2)	70.7 (29)	66.7 (25)	3.1 (-5.9; 12.0)
Helpfullness	0.4 (-6.0; 6.8)	74.1 (23)	73.1 (25)	1.4 (-6.3; 9.0)	68.3 (24)	68.9 (23)	-2.0 (-10.7; 6.9)
SATISFACTION WITH CARE							
Doctor interpersonal skills	0.3 (-5.5; 6.2)	76.9 (21)	76.3 (18)	-1.0 (-7.5; 5.5)	75.6 (22)	73.9 (20)	1.3 (-5.9; 8.4)
Nurse interpersonal skills	-2.9 (-8.5; 2.8)	76.1 (21)	76.0 (19)	-1.9 (-8.2; 4.4)	72.4 (22)	73.9 (23)	-1.6 (-8.6; 5.4)
Exchange information caregiver	-1.5 (-6.8; 3.8)	67.0 (21)	66.7 (19)	-1.8 (-8.1; 4.5)	64.8 (21)	61.8 (20)	0.8 (-6.5; 8.1)
General satisfaction with care	-0.2 (-5.3; 5.0)	78.3 (21)	76.7 (19)	-0.6 (-6.7; 5.5)	77.6 (20)	75.9 (18)	0.5 (-6.4; 7.4)
ILLNESS PERCEPTIONS							
How much illness affects life	0.1 (-0.7; 0.8)	6.3 (2.5)	6.1 (2.6)	0.3 (-0.5; 1.1)	5.1 (2.7)	5.3 (2.7)	-0.1 (-1.0; 0.8)
How long illness will continue	0.7 (-0.1; 1.4)	5.7 (2.5)	5.4 (2.8)	0.7 (-0.2; 1.7)	5.9 (3.3)	5.4 (3.1)	1.0 (-0.0; 2.1)
How much control over illness	-0.2 (-1.0; 0.6)	4.5 (3.1)	4.8 (2.8)	-0.4 (-1.3; 0.6)	4.7 (3.5)	4.5 (2.8)	0.2 (-0.9; 1.3)
How much treatment helps to cure	**-1.0** (-1.6; -0.4)**	7.2 (2.3)	7.8 (1.8)	**-0.8* (-1.6; -0.1)**	6.7 (2.9)	7.2 (2.4)	**-0.9* (-1.8; -0.1)**
How much symptoms experienced	0.1 (-0.7; 0.8)	5.3 (2.5)	5.1 (1.6)	0.5 (-0.3; 1.3)	4.0 (2.5)	4.8 (2.6)	-0.5 (-1.4; 0.4)
How concerned about illness	0.3 (-0.5; 1.0)	6.2 (2.7)	5.8 (2.8)	0.7 (-0.1; 1.6)	5.1 (2.8)	5.6 (3.0)	-0.4 (-1.3; 0.5)
How well understand illness	-0.2 (-1.0; 0.6)	6.8 (2.7)	6.5 (2.6)	0.4 (-0.6; 1.4)	6.4 (3.2)	6.8 (2.8)	-0.5 (-1.6; 0.6)
How much affects emotionally	0.2 (-0.6; 1.0)	5.3 (2.7)	5.1 (2.7)	0.3 (-0.5; 1.2)	4.4 (2.7)	4.8 (2.7)	-0.2 (-1.2; 0.7)
HEALTH CARE UTILIZATION							
Visits medical specialist past 6 months	-1.2 (-2.5; 0.1)	7.0 (4.2)	8.5 (6.2)	-1.5 (-3.2; 0.3)	4.9 (3.5)	7.6 (9.4)	**-2.5* (-4.5; -0.4)**
Visits primary care physician past 6 months	-0.5 (-1.2; 0.2)	3.1 (3.5)	3.6 (3.1)	-0.3 (-1.3; 0.7)	2.6 (2.6)	3.1 (3.4)	-0.4 (-1.6; 0.8)

Note: Linear multilevel regression analyses were performed, adjusted for age, time since diagnosis, marital status, socio-economic status, employment, comorbidities, stage, and treatment. Overall analyses report the results of the main effect of the intervention without the interaction between trial arms and time in the model. Crude means and standard deviations (SD) are reported for SCP Care and Usual Care. Unstandardized betas and confidence intervals are reported for SCP Care (ref=Usual Care). Intention To Treat analyses compared all respondents in the SCP care arm to all respondents in the usual care arm. EORTC-QLQ-INFO25 and EORTC-IN-PATSAT32 scales ranging from 0-100: higher scores reflect better perceived information and care received. B-IPQ scale ranging from 1-10: higher scores indicate more endorsement of that item. Health care utilization shows patients' reported frequency of cancer-related contact with their medical specialist or primary care physician in the past 6 months. * p<0.05 ** p<0.01

Table 3: Continued

	Overall	After 12 months (N=100)			After 24 months (N=75)		
	Beta (95%CI)	M (SD) SCP care	M (SD) Usual care	Beta (95%CI)	M (SD) SCP care	**M (SD) Usual care**	**Beta (95%CI)**
INFORMATION PROVISION							
Disease	0.0 (-6.0; 6.0)	61.2 (19)	59.1 (22)	-1.8 (-10.0; 6.4)	55.7 (21)	59.8 (25)	-5.4 (-14.2; 3.5)
Medical tests	-2.4 (-8.9; 4.1)	70.5 (20)	70.5 (23)	-2.0 (-11.0; 6.9)	62.8 (22)	71.0 (24)	-8.8 (-18.5; 0.9)
Treatment	-1.8 (-7.8; 4.2)	53.7 (23)	56.4 (20)	-3.8 (-12.1; 4.5)	48.1 (24)	51.8 (20)	-2.6 (-11.6; 6.5)
Other services	-5.5 (-12.3; 1.3)	37.2 (26)	39.2 (25)	-6.7 (-16.2; 2.8)	27.4 (23)	34.5 (20)	**-11.2* (-21.5; -0.9)**
Places to go	1.6 (-6.7; 9.8)	39.4 (37)	27.5 (33)	4.3 (-8.6; 17.1)	28.5 (32)	20.3 (26)	2.5 (-11.5;16.5)
Things to do	-0.7 (-8.9; 7.5)	37.4 (29)	44.3 (29)	-10.0 (-22.8; 2.7)	31.0 (29)	37.0 (27)	-9.3 (-23.1; 4.6)
Satisfaction	1.8 (-5.0; 8.7)	70.6 (21)	67.2 (23)	0.2 (-9.4; 9.7)	64.4 (25)	63.7 (24)	1.9 (-8.4; 12.2)
Helpfullness	0.4 (-6.0; 6.8)	71.9 (23)	66.1 (23)	3.2 (-6.3; 12.7)	66.7 (26)	69.8 (19)	-1.4 (-11.7; 9.0)
SATISFACTION WITH CARE							
Doctor interpersonal skills	0.3 (-5.5; 6.2)	78.6 (18)	72.2 (20)	3.3 (-4.3; 10.8)	74.3 (19)	72.1 (21)	0.2 (-8.3; 7.9)
Nurse interpersonal skills	-2.9 (-8.5; 2.8)	72.7 (17)	75.7 (21)	-8.9 (-20.6; 2.7)	67.8 (22)	83.1 (14)	**-12.6* (-24.8; -0.4)**
Exchange information caregiver	-1.5 (-6.8; 3.8)	64.7 (21)	60.7 (23)	-1.3 (-9.6; 7.0)	59.2 (18)	63.2(21)	-5.6 (-14.6; 3.4)
General satisfaction with care	-0.2 (-5.3; 5.0)	70.7 (17)	64.2 (19)	4.5 (-3.3; 12.3)	61.6 (19)	66.5 (21)	-7.0 (-15.5; 1.5)
ILLNESS PERCEPTIONS							
How much illness affects life	0.1 (-0.7; 0.8)	5.2 (2.5)	5.3 (2.8)	-0.0 (-1.0; 1.0)	5.6 (2.5)	4.9 (2.8)	0.2 (-0.8; 1.3)
How long illness will continue	0.7 (-0.1; 1.4)	5.6 (3.0)	5.9 (3.5)	0.3 (-0.8; 1.5)	6.7 (3.3)	6.1 (3.7)	0.6 (-0.7; 1.8)
How much control over illness	-0.2 (-1.0; 0.6)	4.0 (2.6)	4.2 (3.1)	-0.2 (-1.4; 0.9)	4.1 (3.0)	4.3 (3.1)	-0.1 (-1.4; 1.2)
How much treatment helps to cure	**-1.0** (-1.6; -0.4)**	6.4 (2.7)	7.2 (2.5)	**-1.4** (-2.3; -0.4)**	6.7 (2.2)	7.2 (2.3)	-0.7 (-1.8; 0.3)
How much symptoms experienced	0.1 (-0.7; 0.8)	4.5 (2.8)	4.8 (2.8)	-0.1 (-1.1; 0.9)	4.2 (2.4)	4.8 (2.9)	0.8 (-1.8; 0.4)
How concerned about illness	0.3 (-0.5; 1.0)	5.8 (2.7)	5.6 (3.1)	0.1 (-0.9; 1.2)	5.9 (2.5)	5.2 (2.8)	0.5 (-0.6; 1.6)
How well understand illness	-0.2 (-1.0; 0.6)	6.0 (3.1)	6.5 (3.1)	-0.8 (-1.9; 0.4)	6.9 (3.4)	6.6 (3.1)	0.2 (-1.1; 1.5)
How much affects emotionally	0.2 (-0.6; 1.0)	5.3 (2.5)	5.0 (3.0)	0.4 (-0.6; 1.4)	5.4 (2.6)	4.2 (2.5)	0.8 (-0.3; 2.0)
HEALTH CARE UTILIZATION							
Visits medical specialist past 6 months	-1.2 (-2.5; 0.1)	3.4 (2.6)	3.6 (2.9)	0.2 (-2.0; 2.5)	2.9 (2.2)	3.2 (2.4)	-0.3 (-2.8; 2.2)
Visits primary care physician past 6 months	-0.5 (-1.2; 0.2)	0.9 (1.4)	2.3 (4.1)	-1.2 (-2.6; 0.2)	0.6 (1.2)	0.9 (1.4)	-0.3 (-1.8; 1.2)

Note: Linear multilevel regression analyses were performed, adjusted for age, time since diagnosis, marital status, socio-economic status, employment, comorbidities, stage, and treatment. Overall analyses report the results of the main effect of the intervention without the interaction between trial arms and time in the model. Crude means and standard deviations (SD) are reported for SCP Care and Usual Care. Unstandardized betas and confidence intervals are reported for SCP Care (ref=Usual Care). Intention To Treat analyses compared all respondents in the SCP care arm to all respondents in the usual care arm. EORTC-QLQ-INFO25 and EORTC-IN-PATSAT32 scales ranging from 0-100: higher scores reflect better perceived information and care received. B-IPQ scale ranging from 1-10: higher scores indicate more endorsement of that item. Health care utilization shows patients' reported frequency of cancer-related contact with their medical specialist or primary care physician in the past 6 months. * p<0.05 ** p<0.01

DISCUSSION

In the present trial among ovarian cancer patients, SCPs had no beneficial effect on satisfaction with information provision and care. Instead, receiving an SCP caused less trust that the treatment would help to cure the disease. These current results are in line with earlier findings from the ROGY care trial among endometrial cancer patients.[11]

Prior findings from our trial among endometrial cancer patients showed no effect of SCPs on satisfaction with information provision and care, but patients were more concerned about their illness, more affected emotionally and they experienced more symptoms.[11] In the current study among ovarian cancer patients, no effect of SCPs was found on concerns, emotional impact or symptoms experienced. This may be due to existing information provision that in most cases already explains about the poor prognosis and extensive treatment regimens generally needed for ovarian cancer. From oncology practice, we know that in endometrial cancer, treatments are often less extensive and therefore generally less information is provided. On the other hand, ovarian cancer patients who received an SCP had less trust that the treatment would help to cure the disease. This may be explained by the fact that ovarian cancer generally has a poor prognosis, and information provided in the SCP (i.e. on chance of recurrence) may not support the patients' belief that she will be cured. This is negative yet realistic information that the patient otherwise would mostly not receive, as oncology providers are often reluctant to provide such information in order to prevent the patient from negative psychosocial effects.[31] We should take in mind that for patients with an advanced cancer stage and poor prognosis, an SCP provides unfavorable information and may need to be accompanied with more extensive discussion with an oncology provider. Earlier RCTs did not focus on patient populations with advanced stages.[6-8,32]

At this point, we are not sure whether less trust in the treatment is either harmful or beneficial for the patient. If patients incorrectly experience less trust in the treatment, the SCP may unnecessarily accumulate psychosocial distress. However, if less trust is according prospect, patients may be more prepared for potential negative long-term consequences of the disease, such as side effects or a recurrence. Further research is needed to assess the impact of less treatment trust on long-term quality of life, anxiety and depressive symptoms. However, it is important to keep in mind that effect sizes of illness perceptions are small; they did not reach the minimal clinically important difference threshold of 0.5 SD and may therefore be considered not clinically relevant.

In contrast to earlier findings of our trial which showed an increased amount of cancer related contact with the primary care physician in endometrial cancer patients who received an SCP, we found that ovarian cancer patients receiving an SCP reported less

contact with the medical specialist in the six months after diagnosis. Possibly, ovarian cancer patients receiving an SCP have lower needs of contact with their medical specialist because questions or concerns regarding the illness are already covered in the SCP. Another explanation of this finding may be that the patients in the SCP care arm less often received chemotherapy and had therefore less contact with the medical specialist. Further, our results are based on self-reported health care use; exact registrations of hospital visits would be more reliable and may show different results. For instance, patients in the SCP care arm completed the first questionnaire a longer period of time after diagnosis compared to patients in the usual care arm. The lower self-reported health care use in the SCP care arm at 6 months after diagnosis may therefore be explained by time since treatment completion. However, we adjusted for this in our analysis and results remained similar.

Strikingly, we found that patients in the usual care arm reported a higher receipt of information on other services at 6 and 24 months after diagnosis, and higher satisfaction with the interpersonal skills of the nurses. These findings may be explained by the pragmatic approach of our trial; we did not control the existing information provision or care in the usual care arm. It is therefore possible that in the usual care hospitals certain aspects of information provision were perceived better compared to the intervention hospitals. Further, 18% of the patients in the usual care arm reported receipt of an SCP, although SCP provision was impossible in these hospitals.[10] Probably, these patients have perceived other information provision as an SCP.

An advantage of our pragmatic design is that oncology providers were free to choose how SCP provision was implemented, reflecting real-life clinical practice. Inevitably, this resulted in variance across the hospitals with respect to how the SCP was provided, ranging from extensively discussing the SCP with the patient to just handing one without discussion. Our trial did not aim to assess the impact of an SCP that is extensively discussed with the patient. Therefore we did not measure the extent to which the SCP was discussed with each patient. However, as shown in a recent trial among breast cancer patients, combining an SCP with a behavioral intervention using motivational interviewing techniques may actually be beneficial for patients.[32] Possibly, this would be even more beneficial in patients with advanced cancer stages as they generally have higher supportive care needs.[33] Future research is needed to assess the impact of an SCP combined with a behavioral intervention in larger samples and various cancer types.

Among the few RCTs that assessed the impact of SCPs on patient reported outcomes.[6-8,32] the ROGY care trial was the first with a pragmatic cluster randomized design, which maximizes external validity and prevents contamination between trial arms.[10] Another unique feature of the trial was that SCPs could be automatically generated through the

online registration system ROGY, which minimizes the time needed for SCP provision and allows for provision of updated follow-up SCPs. However, only 16% of the patients in this study reported receipt of an updated SCP. This shows that SCPs were not always updated by the oncology provider when there was a recurrence, changes in treatment or oncology provider. This is probably due to difficulties with finding time to discuss the SCP.[14]

A limitation of our study is the small number of patients in our SCP care arm. This was mainly due to one large intervention hospital which, in contrast to endometrial cancer patients, did not include ovarian cancer patients in the trial. Nevertheless, our overall analysis had sufficient power to detect a minimum effect size of 0.5. However, effect sizes in our analyses turned out to be much smaller, meaning that the power of our analysis was too small to detect those small effects. Future studies aiming to detect an effect of SCPs on the outcomes used in the current analyses, should use a larger sample size. However, one may argue that detecting an effect with an effect size smaller than 0.5 is not clinically relevant.

In this study, a substantial number of patients were lost to follow-up during our two-year trial. Because of the relatively low survival in ovarian cancer, lost to follow-up was for a large part caused by death or ill-health. This resulted in a selection of patients in our follow-up analysis, who had lower cancer stages. However, the effect of the SCP was similar for patients lost to follow-up and patients who completed participation in our trial.

Further, as shown in a process evaluation of our trial[18] SCPs were generated (i.e. the oncology provider clicked the SCP button in the ROGY system) for 82% of the ovarian cancer patients. However, we found that only 66% of the ovarian cancer patients in the SCP care arm actually reported SCP receipt. Thus, for 16% of the patients we are not sure what happened: the oncology provider did not hand over the SCP to the patient, or the patient might have forgotten her receipt of an SCP. Among endometrial cancer patients, the number of patients that reported receipt of an SCP was higher (74%), probably because most of the oncology care was provided by an oncology provider that provided the SCP in our trial (i.e. gynecologist, gynecologic oncologist or oncology nurse), while in ovarian cancer patients oncology care is for a large part provided by medical oncologists who were not instructed to provide SCPs.

Due to the pragmatic nature of the trial, not all trial participants received an SCP, reflecting real-life clinical practice. A process evaluation of our trial[18] showed that certain patients less often received an SCP (i.e. older patients and patients with a distressed personality). Current results may therefore not be fully generalizable to the full patient population. Possibly, SCPs have a higher impact on threatening illness perceptions in patients with a distressed personality, as they tend to experience more negative emotions without

sharing these emotions with others.[18] Unfortunately, we could not assess if there was a selection bias in patient recruitment in the SCP care arm compared to the usual care arm, as no data was available on proportions of patients recruited versus not recruited. We did not find statistical differences in baseline characteristics between the trail arms, but our trial was not powered to detect differences in the categorical baseline variables. Possibly, patients in the SCP care arm were somewhat healthier compared to patients in the usual care arm (i.e. lower FIGO stage and less often received chemotherapy), which may have underestimated true effects of the SCPs to some extent. For instance, the impact of SCPs on illness perceptions may be worsened in unhealthier patients. However, we do not assume that we would find an effect on satisfaction with information provision or satisfaction with care, as no trend is observed in current results.

In order to assess the impact of SCPs in a situation where all patients would receive one, we conducted a per protocol analyses in addition to an intention to treat analyses. To make sure of this, we only compared the patients in the SCP care arm that reported SCP receipt, to all patients in the usual care arm. However, results did not differ much between intention to treat and per protocol analyses.

In conclusion, the present study confirms earlier findings from the ROGY care trial that SCPs did not increase satisfaction with information provision or care. Instead, SCPs led to a lower trust in the treatment among ovarian cancer patients which might reflect a more realistic perspective on the treatments effects, while among endometrial cancer patients the SCPs seemed to unnecessarily cause higher concerns, emotional impact and symptom awareness. Our trial results suggest that patients may not benefit from an SCP as was proposed by the IOM. However, the benefit of an SCP combined with a behavioral intervention needs to be further explored.

REFERENCES

1. Rowland JH, Kent EE, Forsythe LP, et al. Cancer survivorship research in Europe and the United States: where have we been, where are we going, and what can we learn from each other? *Cancer.* 2013;119(S11):2094-2108.
2. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment–psychosocial and behavioural issues in cancer survivorship research and practice. *European Journal of Cancer Supplements.* 2014;12(1):54-64.
3. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
4. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
5. Klemanski DL, Browning KK, Kue J. Survivorship care plan preferences of cancer survivors and health care providers: a systematic review and quality appraisal of the evidence. *Journal of Cancer Survivorship.* 2016;10(1):71-86.
6. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
7. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment.* 2013;138(3):795-806.
8. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
9. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. *Journal of Cancer Survivorship.* 2015;9(4):683-691.
10. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2011;12:256.
11. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
12. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA: A cancer journal for clinicians.* 2015.
13. Netherlands CR. Netherlands Cancer Registry. 5-year survival of ovarian cancer patients diagnosed between 2008 and 2012. URL www.cijfersoverkanker.nl [accessed 1/4/2016]. 2014.
14. Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, van de Poll-Franse LV, Kruitwagen RF. Oncology providers' evaluation of the use of an automatically generated cancer survivorship care plan: longitudinal results from the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Jun 2014;8(2):248-259.
15. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *European Journal of Cancer.* 2011;47(14):2188-2194.
16. Campbell MK, Piaggio G, Elbourne DR, Altman DG, . Consort 2010 statement: extension to cluster randomized trials. *BMJ.* 2012;345: e5661.
17. Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, van de Poll-Franse LV, Kruitwagen RF. Oncology providers' evaluation of the use of an automatically generated cancer survivorship care plan: longitudinal results from the ROGY Care trial. *J Cancer Surviv.* 2014;8 (2):248-259.
18. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Factors influencing implementation of a survivorship care plan-a quantitative process evaluation of the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Aug 1 2016.
19. Ezendam NP, Nicolaije KA, Kruitwagen RF, et al. Survivorship Care Plans to inform the primary care physician: results from the ROGY care pragmatic cluster randomized controlled trial. *Journal of cancer survivorship : research and practice.* Dec 2014;8(4):595-602.

20. Hewitt M, Greenfield S, Stovall E, eds. *From cancer patient to cancer survivor: lost in transition*. Washington, DC: National Academies Press; 2006.
21. Ganz PA, Hahn EE. Implementing a survivorship care plan for patients with breast cancer. *J Clin Oncol* 2008;26:759-767.
22. Netherlands Cancer Registry (NCR). Netherlands Cancer Registration *URL: http://www.cijfersoverkanker.nl/ [accessed 30-01-2015]* 2015.
23. Van Duijn C, Keij I. Sociaal-economische status indicator op postcode niveau. *Maandstatistiek van de bevolking*. 2002;50(2):32-35.
24. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: A new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003;49:156-163.
25. Arraras JI, Greimel E, Sezer O, et al. An international validation study of the EORTC QLQ-INFO25 questionnaire: an instrument to assess the information given to cancer patients. *Eur J Cancer* 2010;46:2726-2738.
26. Bredart A, Bottomley A, Blazeby JM, et al. An international prospective study of the EORTC cancer in-patient satisfaction with care measure (EORTC IN-PATSAT32). *Eur J Cancer* 2005;41:2120-2131.
27. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res*. 2006;60:631-637.
28. Twisk JWR. *Applied Multilevel Analysis: A Practical Guide for Medical Researchers*. New York: Cambridge University Press 2006.
29. Peters SAE, Bots ML, den Ruijter HM, et al. Multiple imputation of missing repeated outcome measurements did not add to linear mixed-effects models. *Journal of Clinical Epidemiology*. 2012;65:686-695.
30. Beunckens C, Molenberghs G, Kenward MG. Direct likelihood analysis versus simple forms of imputation for missing data in randomized clinical trials. *Clinical Trials*. 2005;2:379-386.
31. Cox A, Faithfull S. 'They're survivors physically but we want them to survive mentally as well': health care professionals' views on providing potential late effect information. *Support Care Cancer*. 2013;21:2491-2497.
32. Kvale EA, Huang CS, Meneses KM, et al. Patient-centered support in the survivorship care transition: Outcomes from the Patient-Owned Survivorship Care Plan Intervention. *Cancer*. Oct 15 2016;122(20):3232-3242.
33. Sanson-Fisher R, Girgis A, Boyes A, Bonevski B, Burton L, Cook P. The unmet supportive care needs of patients with cancer. Supportive Care Review Group. *Cancer*. Jan 01 2000;88(1):226-237.

Chapter 4

Patients' information coping styles influece the benefit of a survivorship care plan in the ROGY Care Trial: new insights for tailored delivery

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ABSTRACT

Background: In efforts to improve implementation of Survivorship Care Plans (SCPs), we aim to assess whether the impact of SCPs on patient reported outcomes is different in patients with an information seeking ('monitoring') versus an information avoiding ('blunting') coping style.

Methods: In the ROGY Care Trial, twelve hospitals in the Netherlands were randomized to 'SCP care' or 'usual care'. All newly diagnosed endometrial and ovarian cancer patients in the 'SCP care' arm received a SCP that was automatically generated by the oncology provider through the web-based Registrationsystem Oncological GYnecology (ROGY). Outcomes (satisfaction with information provision and care, illness perceptions and health care use) were measured directly after initial treatment and after 6, 12 and 24 months. Information coping style was measured at 12 months after initial treatment.

Findings: Among patients with a 'monitoring' coping style (N=123), those in the 'SCP care' arm reported higher satisfaction with information provision (73.9 vs. 63.9, p=0.04) and care (74.5 vs. 69.2, p=0.03) compared to those in the 'usual care' arm. Among patients with a 'blunting' coping style (N=102), those in the 'SCP care' arm reported a higher impact of the disease on life (5.0 vs 4.5, p=0.02) and a higher emotional impact of the disease (5.4 vs. 4.2, p=0.01) compared to those in the 'usual care' arm.

Conclusions: SCPs may be beneficial for patients who desire information about their disease, while SCPs may be less beneficial for patients who avoid medical information, suggesting a need for tailored SCP delivery to improve survivorship care.

Trial Registration: clinicaltrials.gov Identifier: NCT01185626

INTRODUCTION

For more than a decade, Survivorship Care Plans (SCPs) have been broadly endorsed as a means to improve care coordination and to address the unmet information needs in the growing population of cancer survivors.[1] Since the first recommendation by the Institute of Medicine in 2006[1], SCPs have been the focus of survivorship care research.[2] Despite these efforts, the evidence base for the impact of SCPs among cancer survivors is still inconclusive and directions for future implementation of SCPs remain under debate.[3] Randomized controlled trials (RTCs) failed to identify benefits of SCP delivery on patient satisfaction, quality of life and distress in various patient populations, including breast[4,5], gynecological[6-8], colorectal[9] and prostate[10] cancer. However, SCPs may be beneficial for selected subgroups of survivors, such as underserved populations[11] and patients who do not use other sources of medical information such as the internet[12], reflecting that we should focus on those individuals that benefit most from SCPs.

Ample research in health communication demonstrates that individuals respond differently to medical information, due to different coping strategies.[13,14] Miller identified two main information coping styles for dealing with health threats such as cancer: 'monitoring' and 'blunting'.[15] Monitors typically seek for information relevant for them with regard to their health threat, while blunters prefer to avoid medical information and distract from it. Monitors report more anxiety related to their cancer treatment,[16] they desire more voluminous and detailed information about their disease and tend to be more often dissatisfied with the information they receive.[17] Conversely, among blunters, excessive information before a diagnostic procedure resulted in more self-reported tension, depression and physical discomfort among patients with a blunting coping style.[18] Hence, in a sample of gynecologic patients at risk of cancer, stress reduction appears to be most optimal for monitors when they receive much information, while blunters respond better when they receive minimal information.[19] These findings suggest that SCPs may be more beneficial for cancer survivors with a monitoring coping style compared to those with a blunting coping style.

In efforts to improve future implementation of SCPs, we aim to assess whether information coping style moderates the impact of SCPs on patient reported outcomes among gynecological cancer patients in the pragmatic cluster-randomized ROGY Care Trial, including satisfaction with information provision and care, illness perceptions and health care use. In main analyses of this trial, the overall effects of SCPs among endometrial and ovarian cancer patients were assessed. We demonstrated that SCPs did not improve satisfaction with information provision and care, but increased worry, emotional impact and experienced symptoms among endometrial cancer patients[7], and decreased trust in the treatment among ovarian cancer patients.[8] Yet, we hypothesize that SCPs have a

positive effect on satisfaction with information provision and care, and health care use in patients with a monitoring coping style but not with a blunting coping style, whereas SCPs may increase threatening illness perceptions in patients with a blunting coping style but not with a monitoring coping style.

METHODS

Design

The ROGY Care Trial is a pragmatic cluster-randomized controlled trial that aimed to assess the impact of automatically generated SCPs on patient reported outcomes among endometrial and ovarian cancer patients during 2-year follow-up. Twelve hospitals in the Netherlands were randomized to either 'SCP care' or 'usual care'. The trial was centrally approved by a Medical Research Ethics Committee and is registered as NCT01185626 in clinicaltrials.gov. Further details about the design are described in the trial protocol.[20]

Participants and recruitment

After initial treatment, all patients newly diagnosed with endometrial cancer between April 2011 and October 2012, or ovarian cancer between April 2011 and March 2014, were invited to participate by their own gynecologist with a letter and an informed consent form. After consent, questionnaires were sent to the patient after treatment, and after 6, 12 and 24 months. Because of the pragmatic nature of the trial, exclusion criteria were limited. Only patients with a borderline ovarian tumor, undergoing palliative care or unable to complete a Dutch questionnaire were excluded from participation.[20] The current analysis only includes patients who completed the questionnaire assessing information coping style at 12 months after initial treatment (Appendix I). Primary effects of SCPs on patient reported outcomes in endometrial[7] and ovarian[8] cancer patients have been described previously.

Randomization and blinding

Randomization was performed via a table of random numbers, by an independent researcher blinded to the identity of the hospitals. Patients, but not oncology providers or researchers assessing the outcomes, were blinded to trial assignment.[20]

SCP care versus usual care

In the hospitals providing 'usual care', standard care was provided in accordance to the Dutch oncology guidelines (www.oncoline.nl). In the 'SCP care' hospitals, all oncology providers (gynecologist/gynecologic oncologist and oncology nurses) were instructed to provide an SCP to patients at the consultation where the results of histopathology and (adjuvant) treatment plan were discussed (i.e. 7-14 days after surgery). An updated version of the SCP could optionally be discussed in a follow-up consultation. Practical

guidelines were given on the components of the SCP that should minimally be discussed with each patient during the consultation.. The SCP was based on the Dutch translation of the American Institute of Medicine (IOM) SCP template,[1] adjusted to the local situation.[20] Texts of the SCP were based on pilot-tested patient education material from the Dutch Cancer Society. In addition, the SCP was pilot-tested on patients with a low/intermediate educational level to ensure that the SCP was understandable. The SCP contained a treatment summary and a follow-up care plan, including detailed information on short- and long-term effects of the treatments received, effects on social and sexual life, possible signs of recurrence and secondary tumors, and information on rehabilitation, psychosocial support, and supportive care services. Details about the intervention[20] and implementation[21] have been described previously.

Measures

Age, socio-economic status (SES) and clinical data were obtained from the Netherlands Cancer Registry (NCR).[22] SES was based on postal code of the residence area of the patient, combining aggregated individual fiscal data on the economic value of the home and household incomes[23] and categorized into low, medium or high. Additional socio-demographic information was assessed in the first questionnaire. Marital status ('married/living together' versus 'divorced/widowed/never married') and employment status ('having a paid job' versus 'not having a paid job') were dichotomized. Comorbidity was assessed by the adapted Self-administered Comorbidity Questionnaire (SCQ), and categorized into no comorbidities, one comorbidity or more than one comorbidity.[24] Disease-related internet use and receipt of an SCP ("Did you receive a Survivorship Care Plan?") were dichotomous measures.

Information coping style was assessed using the shortened version of The Threatening Medical Situations Inventory (TMSI)[25], consisting of two hypothetical descriptions of medical situations. The internal consistency of the monitoring (Cronbach's alpha=0.79) and blunting (Cronbach's alpha=0.73) subscales were good and test-retest reliability has been established as sufficient for both scales (Pearson correlations 0.64-0.83).[25,26] As described previously,[15] a sum score was calculated by subtracting the blunting subscale from the monitoring subscale. Individuals with sum scores below or equal to the median were categorized as 'monitors' and individuals with scores above the median were categorized as 'blunters'.

Outcome scales were assessed in each questionnaire. Information provision was measured with the EORTC-QLQINFO25,[27] using four multi-item subscales (information about the disease, medical tests, treatment and other care services) and four single-item scales (information about different places of care, things you can do to help yourself get well, satisfaction with the information, helpfulness of the information). Internal consistency of the scales in our sample (Cronbach's alphas 0.75-0.90) were good. Test-retest reliability

(intraclass correlations 0.71-0.91) has been established as good previously.[27] Satisfaction with care was assessed with the EORTC INPATSAT32 that was adjusted to make the questionnaire appropriate for use during survivorship care[28] using two multi-item scales (doctor's interpersonal skills and nurses' interpersonal skills) and two singe-item scales (exchange of information between caregivers and general satisfaction with care). Internal consistency of the scales in our sample (Cronbach's alphas 0.93-0.94) were good. Previously, test-retest reliability (intraclass correlations 0.66-0.85) have been established as good.[28] Illness perception was assessed with the Brief Illness Perception Questionnaire (B-IPQ).[29] Scales included eight single-item scales. Test-retest reliability (Pearson correlations 0.42-0.75) was fair to good.[29] Health care use was assessed by the number of visits to a medical specialist or primary care physician in relation to cancer in the past 6 months.

Statistical Analysis

Statistical analyses were conducted using Statistical Analysis System (SAS) version 9.4. (SAS Institute, Cary, NC, 1999). Differences in characteristics between patients included in the analyses and lost to follow-up, between trial arms, and between patients with monitoring and blunting coping styles were compared using t-tests for normally distributed continuous variables, Mann-Whitney U-tests for not-normally distributed variables and chi-square tests for categorical variables.

Linear multilevel regression analysis was performed to assess the moderating effect of information coping style on the impact of SCPs on patient reported outcomes. A random intercept on the patient-level was included in the model to adjust for intra-dependency between repeated measures. [30] Random intercepts on the hospital-level (ICCs<0.16) and random-slopes on the patient-level (ICCs<0.14) were not included because they did not improve the models.[30] To assess the moderating effect of information coping style, an interaction term of information coping style and trial arm, and all a priori-selected covariates (i.e. cancer type, age, time since diagnosis, marital status, socio-economic status, employment, comorbidities, stage, and treatment) were added to the model. Dependent variables were the information provision and care-, illness perceptions-, and health care utilization-scales. For outcome scales where the interaction term of coping style and trial arm was significant, stratified analyses were by information coping style. For all analyses, patients in the 'SCP care' arm were compared to all patients in the 'usual care' arm (Intention-to-treat analysis). In addition, per-protocol analyses were conducted to compare patients in the 'SCP care' arm who reported having received an SCP to all patients in the usual care arm, because no SCPs were provided in the hospitals in the usual care arm. Interactions with cancer type were assessed by a three-way interaction of cancer type, coping style and trial arm. Prior analyses showed a moderating effect of disease-related internet use on the outcome scales[12]. Therefore, we additionally assessed whether there was a three-way interaction between disease-related internet-use, information coping style and trial arm on any of the outcome scales, adjusted for covariates.

RESULTS

In total, 221 endometrial cancer patients and 174 ovarian cancer patients participated in the trial. As described previously, endometrial cancer patients who did not participate in the trial were older and had higher cancer stages.[7,8] Furthermore, endometrial cancer patients in the 'SCP Care' arm completed the questionnaire later after diagnosis compared to endometrial cancer patients in the 'Usual Care' arm.[7] Ovarian cancer patients in the 'SCP Care' arm had more comorbidities compared to ovarian cancer patients in the 'Usual Care' arm.[8]

Table 1: baseline characteristics of participants lost to follow-up versus participants included in analysis, stratified by cancer type, univariate analyses

	Endometrial cancer patients			Ovarian cancer patients		
	Participants included in analysis (N=131)	Participants lost to follow-up (N=90)	P-value	Participants included in analysis (N=94)	Participants lost to follow-up (N=81)	P-value
Age at first questionnaire						
Mean (SD)	65.9 (8.7)	71.3 (8.4)	**<0.01**	61.9 (9.3)	65.9 (12.7)	**<0.01**
SES[a], n (%)						
High	55 (42)	18 (20)	**<0.01**	39 (41)	29 (36)	0.85
Intermediate	49 (37)	42 (47)		37 (39)	37 (46)	
Low	19 (15)	24 (27)		17 (55)	14 (17)	
Unknown	8 (6)	6 (7)		1 (1)	1 (1)	
Marital status[b], n(%)						
Partner	106 (81)	55 (61)	**<0.01**	74 (79)	57 (70)	0.20
No partner	25 (19)	35 (39)		20 (21)	24 (30)	
Employed, n (%)						
Yes	24 (18)	13 (14)	0.34	33 (35)	18 (22)	0.06
No	98 (75)	66 (73)		61 (65)	63 (78)	
Months from diagnosis, n(%)						
Median (IQR)	3.0 (1.8)	3.0 (1.6)	0.62	2.4 (2.4)	2.8 (2.5)	0.20
FIGO-stage, n (%)						
I	122 (93)	69 (77)	**<0.01**	31 (33)	21 (26)	0.57
II	3 (2)	4 (4)		10 (11)	6 (8)	
III	5 (4)	13 (14)		39 (41)	37 (46)	
IV	1 (1)	4 (4)		14 (15)	16 (20)	
Treatment, n (%)						
Surgery	131 (100)	86 (97)	**0.03**	88 (96)	71 (88)	0.054
Chemotherapy	2 (2)	13 (14)	**<0.01**	71 (75)	64 (79)	0.58
Radiotherapy	42 (32)	33 (37)	0.48			
Comorbidity, n (%)						
None	24 (18)	14 (16)	0.17	29 (31)	27 (33)	0.33
1	29 (22)	26 (29)		33 (35)	20 (25)	
2 or more	77 (59)	46 (51)		31 (33)	34 (42)	

[a]Socio-economic status (SES) was based on postal code of the residence area of the patient. [b]Marital status included: partner = married/living together; no partner = divorced/widowed/never married. The numbers may not always add up to 100, because percentages have been rounded off to whole numbers.

Table 2: characteristics of patients included in analysis stratified by information coping style, univariate analyses

	Monitoring Coping Style (N=123)	Blunting Coping Style (N=102)	P-value
Age at first questionnaire			
Mean (SD)	63.3 (9.1)	65.4 (9.2)	0.10
SES[a], n (%)			
High	54 (44)	41 (40)	0.30
Intermediate	46 (37)	40 (39)	
Low	16 (13)	20 (19)	
Unknown	7 (6)	2 (2)	
Marital status[b], n (%)			
Partner	108 (88)	72 (70)	**<0.01**
No partner	15 (12)	31 (30)	
Employed, n (%)			
Yes	33 (28)	24 (24)	0.46
No	83 (72	76 (76)	
Cancer type, n (%)			
Endometrial	74 (60)	57 (55)	0.46
Ovarian	49 (40)	46 (45)	
Months from diagnosis, n(%)			
Median (IQR)	3.0 (2.0)	2.8 (2.2)	0.77
FIGO-stage, n (%)			
I	80 (65)	74 (72)	0.06
II	8 (7)	5 (5)	
III	22 (18)	22 (21)	
IV	13 (11)	2 (1)	
Treatment, n (%)			
Surgery	120 (98)	100 (98)	0.86
Chemotherapy	42 (34)	31 (30)	0.52
Radiotherapy	15 (17)	27 (19)	0.73
Comorbidity, n (%)			
None	31 (26)	22 (21)	0.86
1	32 (26)	30 (29)	
2 or more	58 (48)	50 (49)	
Disease-related internet use, n(%)			
Yes	67 (54)	36 (35)	**<0.01**
No	56 (46)	66 (65)	

[a]Socio-economic status (SES) was based on postal code of the residence area of the patient. [b]Marital status included: partner = married/living together; no partner = divorced/widowed/never married. The numbers may not always add up to 100, because percentages have been rounded off to whole numbers. Note: The monitoring and blunting groups are not of equal size because 19 patients had a median score on the TMSI.

The current analysis included 131 (59%) endometrial and 95 (55%) ovarian cancer patients who completed the questionnaire at 12 months after treatment (Appendix). Compared to patients lost to follow-up, patients included in the current analysis were younger, and endometrial cancer patients more often had a partner, a higher SES, lower cancer

stages, more often received surgery and less often chemotherapy (Table 1). Patients with a monitoring coping style more often had a partner and more often used the internet to look up medical information compared to patients with a blunting coping style (Table 2). Additional analyses stratified by cancer type showed that ovarian cancer patients with higher cancer stages more often had a monitoring coping style ($p<0.01$). The monitoring and blunting groups are not of equal size because 19 patients had a median score on the TMSI.

There was no significant interaction between cancer type and information coping style for any of the outcome scales. Among both endometrial and ovarian cancer patients, information coping style significantly moderated the impact of SCPs on the outcomes scales shown in Table 3. No moderating effect of information coping style on the impact of SCPs was found on satisfaction with information about medical tests and other services, the interpersonal skills of the doctor, exchange of information between caregivers, perceptions about the timeline, personal control, treatment control, identity, emotions and understanding of the disease, and cancer-related contact with the medical specialist and primary care physician. Crude means at all time points stratified by information coping style and trial arm are shown in Figure 1. Overall, patients with a monitoring coping style were more satisfied with information and care, and had less threatening illness perceptions, compared to patients with a blunting coping style. Stratified multilevel linear regression analyses subsequently showed that among patients with a monitoring coping style, patients in the 'SCP care' arm compared to patients in the 'usual care' arm reported higher receipt of information about treatments (β=8.9, CI=2.2-15.5; $p<0.01$), information about things to do to get well (β=11.6, CI=3.3-19.9, $p<0.01$), satisfaction with information received (β=7.7, CI=0.3-15.1, $p=0.04$), perceived helpfulness of the information received (β=8.4, CI=1.4-15.3, $p=0.02$), and higher general satisfaction with care (β=6.2, CI=0.7; 11.8, $p=0.03$). Among patients with a blunting coping style, patients in the 'SCP care' arm compared to patients in the 'usual care' arm reported a higher impact of the disease on life (β=0.9, CI=0.2-1.7, $p=0.02$) and more concerns about the illness (β=1.1, CI=0.3-1.9, $p=0.01$; Table 3). In addition, a significant three-way interaction was observed between disease-related internet use and information coping style on the 'helpfulness' scale: patients in the 'SCP care' arm with a monitoring coping style who did not use the internet for medical information reported higher helpfulness of the information received (β=14.7, CI=3.4-25.9, $p=0.01$), while patients with a monitoring coping style who did use the internet for medical information did not (β=6.8, CI=-2.6-16.2, $p=0.15$). Per-protocol analysis, comparing patients in the 'SCP Care' arm who reported receipt of an SCP (endometrial, N=60, 87%; ovarian, N=24, 75%) with all patients in the 'Usual Care' arm (endometrial, N=62; ovarian, N=63), showed similar results.

Figure 2

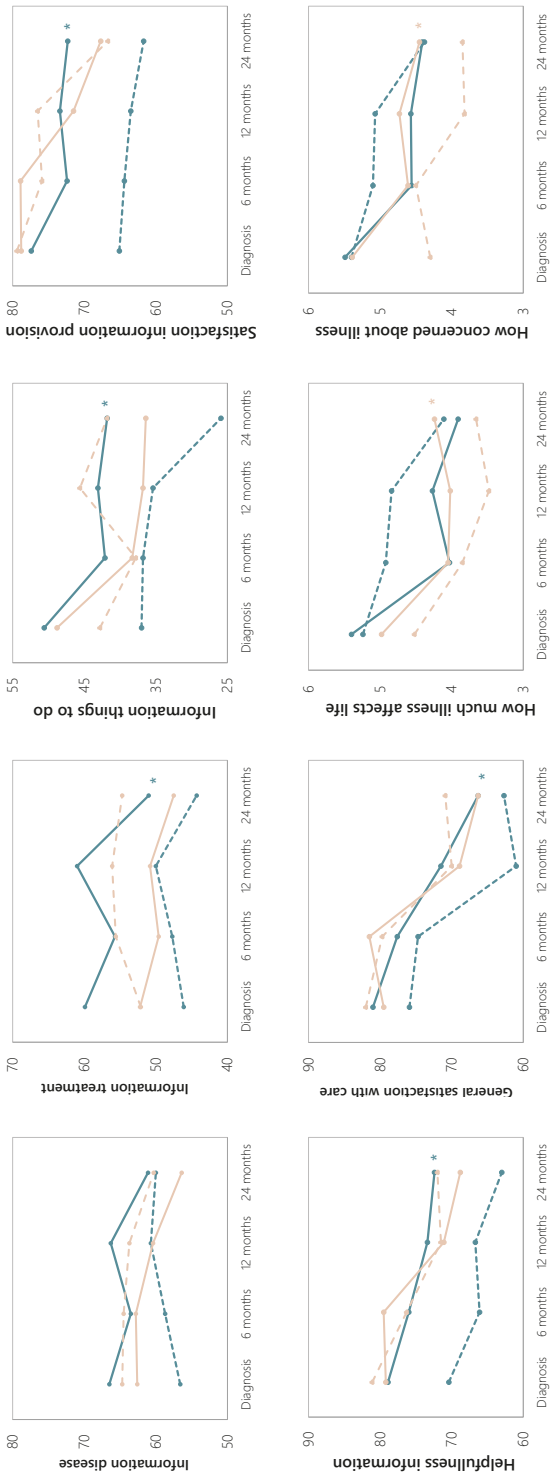

Information disease
Information treatment
Information things to do
Satisfaction information provision
Helpfullness information
General satisfaction with care
How much illness affects life
How concerned about illness
Diagnosis
6 months
12 months
24 months
Monitors - SCP Care
Monitors - Usual Care
Blunters - SCP care
Blunters - Usual Care

Table 3: Effects of the intervention in endometrial and ovarian cancer patients, stratified by information coping style: Intention-to-treat analyses of the overall effects at all time points combined (0, 6, 12 and 24 months)

	Monitoring Coping Style ($N_{subjects}$=123, $N_{observations}$=453)			Blunting Coping Style ($N_{subjects}$=102, $N_{observations}$=374)		
	M (SD) SCP care	M (SD) Usual care	Beta (95%CI)	M (SD) SCP care	M (SD) Usual care	Beta (95%CI)
Satisfaction with information provision						
Disease	64.4 (20)	58.9 (22)	3.5 (-2.7; 9.7)	60.7 (19)	63.5 (23)	-4.8 (-12.5; 2.8)
Treatment	57.0 (24)	47.3 (24)	**8.9 (2.2; 15.5)****	50.2 (24)	54.7 (27)	-3.5 (-12.5; 5.6)
Things to do	44.5 (29)	34.4 (30)	**11.6 (3.3; 19.9)****	40.4 (32)	42.0 (36)	-3.3 (-14.5; 8.0)
Satisfaction	73.9 (23)	63.9 (24)	**7.7 (0.3; 15.1)***	74.5 (21)	75.1 (25)	-1.4 (-9.5; 6.7)
Helpfullness	76.5 (24)	66.8 (22)	**8.4 (1.4; 15.3)***	75.0 (21)	75.4 (24)	-1.2 (-9.1; 6.8)
Satisfaction with care						
Nurse interpersonal skills	75.0 (19)	72.5 (19)	2.9 (-4.3; 10.2)	72.9 (18)	79.9 (20)	-6.5 (-13.2; 0.3)
General satisfaction with care	74.5 (18)	69.2 (19)	**6.2 (0.7; 11.8)***	74.5 (17)	76.1 (20)	-1.7 (-7.2; 2.9)
Illness perceptions						
How much illness affects life	5.4 (2.7)	5.2 (2.8)	0.0 (-0.7; 0.8)	5.0 (2.6)	4.5 (2.6)	**0.9 (0.2; 1.7)***
How concerned about illness	5.5 (2.7)	5.4 (2.9)	0.2 (-0.6; 1.1)	5.4 (2.4)	4.2 (2.6)	**1.1 (0.3; 1.9)***

Note: Linear multilevel regression analyses were performed, stratified by coping style and adjusted for covariates. Only the scales where the interaction term was significant are shown. Analyses report the results of the main effect of the intervention after diagnosis, and after 6, 12 and 24 months, stratified by coping style. Values in bold indicate that the main effect of the intervention was significant in stratified analysis.* p<0.05 ** p<0.01.Crude means and standard deviations (SD) are reported for SCP Care and Usual Care. Unstandardized betas and confidence intervals are reported for SCP Care (ref=Usual Care). EORTC-QLQ-INFO25 and EORTC-IN-PATSAT32 scales ranging from 0-100: higher scores reflect better perceived information and care received. B-IPQ scale ranging from 1-10: higher scores indicate more endorsement of that item.

DISCUSSION

We demonstrated that information coping style moderates the impact of SCPs on patient reported outcomes among gynaecological cancer patients during 2-year follow-up. SCPs appear to improve satisfaction with information and care among patients who desire information about their disease (i.e. monitors), while SCPs seem to increase worry and perceived consequences of the cancer among patients who avoid medical information (i.e. blunters), suggesting a need for tailored delivery of SCPs. No moderating effect of coping style was found on health care use.

In line with literature regarding information coping styles,[17,31] monitors were generally less satisfied with information and care compared to blunters, suggesting that there is room for improvement in patients with a monitoring coping style. Consistent with our hypothesis, SCPs appear to meet the high information needs among monitors by substantially increasing satisfaction in this subgroup (up to 12 points on a 0-100 scale), resulting in similar satisfaction levels as blunters. The other side of the coin is that

blunters, who generally have lower baseline levels of distress,[32] appear to experience increased worry and a higher impact of the disease on life when they receive an SCP. This is consistent with a trial among gynecologic patients that shows that stress reduction among blunters is most optimal when they receive minimal information, as opposed to excessive information.[19] Excessive information may increase arousal among blunters because they are confronted with detailed information about a health threat they did not worry about initially.[18,25] In a sample of gynecologic patients with a blunting coping style, this resulted in self-reported tension, depression and physical discomfort before and during a diagnostic procedure.[19] In contrast, an information brochure for patients undergoing gastrointestinal coloscopy was beneficial in reducing anxiety among patients with a monitoring coping style.[18] Hence, our results are in line with previous health information intervention studies.

In addition, we found that monitors more often used the internet to look up information about their disease compared to blunters, while SCPs appeared most helpful for monitors who did not do so. These findings suggest that SCPs are most valuable for patients that desire information about their disease but do not have access to resources such as the internet. This is in line with earlier findings from our trial that showed that endometrial cancer patients who did not use the internet benefited from SCPs.[12] Notably, prior analyses of our trial demonstrated that more threatening illness perceptions due to the SCP (i.e. more worry, experienced symptoms and lower trust in the treatment) resulted in worse long-term health-related quality of life (HRQoL) and more anxiety.[33] Therefore, we should be aware of potential harmful effects of SCPs in patients with a blunting coping style. Yet, appropriate counselling accompanied with the SCP may reduce the harmful effects on HRQoL.[34]

Interestingly, a previous publication of our trial demonstrated that SCPs increased cancer-related contact with the primary care physician (PCP) among endometrial cancer patients in the first year after treatment[7], which appeared to be related to anxiety.[35] Therefore, we hypothesized that patients with an information coping style, who generally have higher levels of distress, would be more often encouraged to contact their care providers for additional questions and concerns with regard to the SCP. However, we did not find a moderating effect of information coping style on health care use. Perhaps, our findings were diluted by our overall analyses of all time-points combined. Unfortunately, numbers were too small to conduct analyses for each time-point separately.

A limitation of this study includes the selective sample of patients that participated in our trial until at least 12 months after initial treatment to complete the questionnaires included in the current analysis. Patients of higher age and with higher cancer stages were more often lost to follow-up, which may be due to death or ill-health. As a consequence,

the number of patients in the current study was too small to conduct stratified analyses for endometrial and ovarian cancer patients separately, since our trial was powered on analyses of patients that were included from baseline (N=75 per trial arm per cancer type). Although there were no significant interactions with cancer type, the magnitude of the moderating effect of coping style may differ between cancer types. Further, although patients were told they participated in an observational study and response rates were high, patients with a blunting coping style may be underrepresented in our trial because they do not like to be reminded of their cancer[32]. This may have resulted in an underestimation of the potential harmful effects of SCPs among blunters. Further, due to our pragmatic approach, not all patients in the intervention arm reported receipt of an SCP, resulting in an underestimation of the impact when all patients would receive an SCP. Also, unlike most trials, SCPs were provided after initial treatment while some patients were still receiving adjuvant treatment. This may have enlarged the detrimental impact on illness perceptions among blunters because information may have been provided too early.

Another limitation is that information coping style was assessed at 12 months after initial treatment. Although information coping style has shown to be fairly stable over a 1-month period,[25,26] we found that ovarian cancer patients with higher cancer stages more often had a monitoring coping style. Although information coping style has not been associated with disease-related characteristics earlier,[36] our finding may suggest that information coping style has been modified by the experience of a cancer diagnosis, and possibly even by the receipt of an SCP. Yet, the distribution of monitors and blunters did not differ between trial arms, indicating that this probably did not affect our results. It does, however, imply that repeated assessments of information coping style may be needed in order to provide appropriate information when needs have been changed. Further, there is no consensus on whether the outcomes in our analysis such as patient satisfaction are the most relevant in evaluations of SCPs. Future studies may need to focus on more proximal outcomes, such as the understanding of survivorship care issues, care provider roles, self-management and sense of control.[3,37]

It is important to note that the SCPs provided in our trial were extensive documents (i.e. up to 25 pages), containing detailed information about potential long-term and late effects and explicit information about chance of recurrence.[20] The impact of such a voluminous SCP may be much higher compared to treatment summaries or brief SCPs comprising only a couple of pages of information.[38] Yet, these extensive SCPs may principally meet the high information needs of monitors, while brief SCPs may be more beneficial for blunters. The heterogeneity of information needs among cancer survivors may also explain why neither brief nor extensive SCPs appear to be beneficial for patient populations as a whole in current SCP trials.[3] Hence, either withholding information or providing information to all

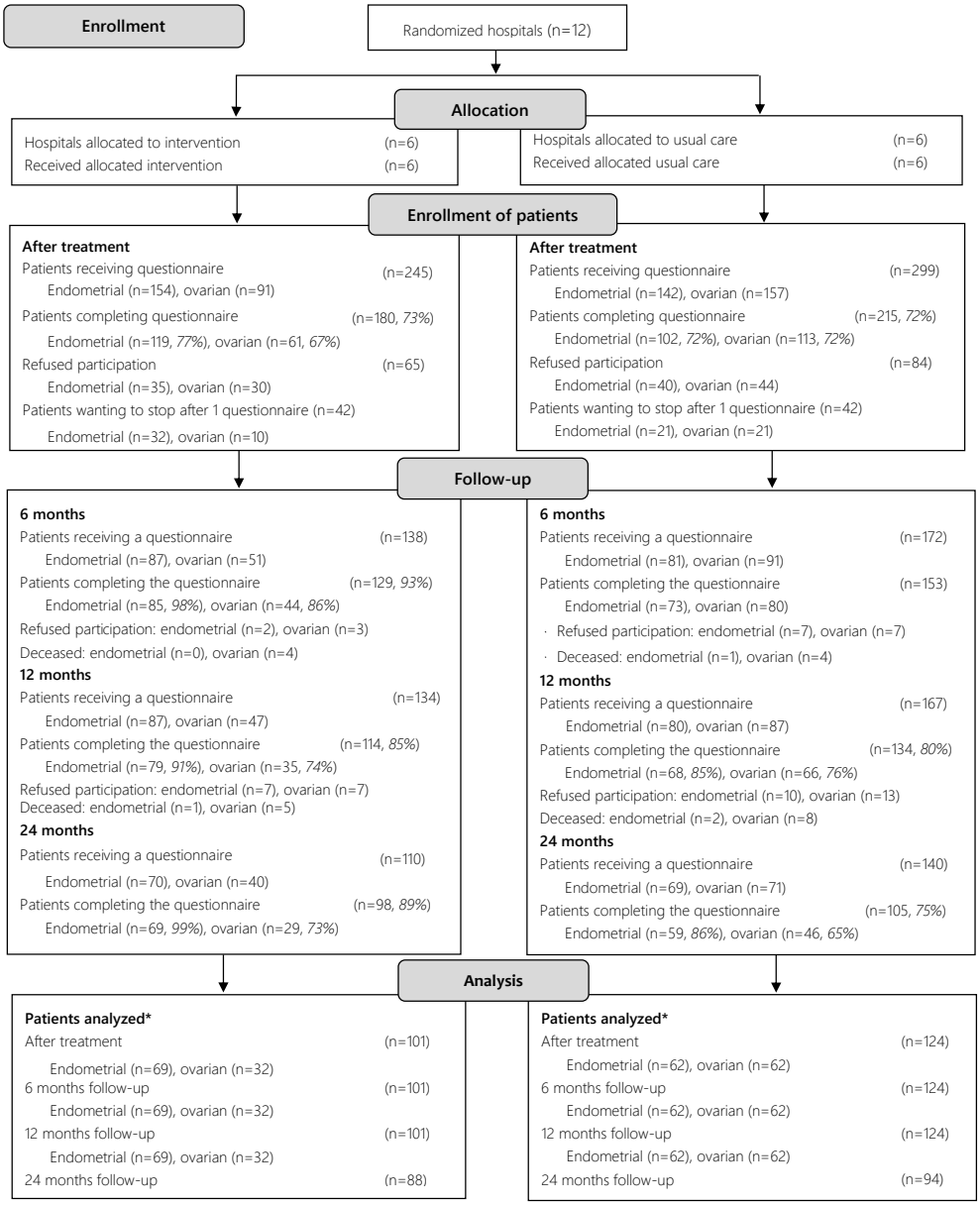
patients uniformly would not utilize patient satisfaction. Rather, we may need to develop distinct templates of SCPs that are tailored to patients' information needs, which would not only improve survivors' outcomes, but may also contribute to a more efficient distribution of the limited resources in survivorship care. Hence, we feel that risk stratification according to information and care needs, similar as applied in individualized follow-up,[39] is needed to accomplish effective and efficient survivorship information provision. Whether SCPs should be individualized according to information 'dose' only (i.e. extensive versus brief SCPs), or also on content (i.e. focus on physical versus psychological aspects)[40], requires further research. Possibly, a simple set of screening questions to determine information needs may be sufficient to utilize tailored SCPs in clinical practice, although repeated assessments may be required as needs may change over time. This may be particularly feasible in a setting where information is provided online. Further, our findings may apply to other types of health information provision, suggesting that careful evaluation of the effects of various information prevision interventions across coping styles is needed before implementation in clinical practice.

Conclusion

Although SCPs may not be helpful for all cancer survivors,[7,8] they appear valuable for subgroups of survivors. We demonstrated that SCPs may be beneficial for patients who desire detailed information about their cancer, while they may be less beneficial and perhaps even harmful for patients who prefer to avoid medical information. Our study emphasizes the need to individualize delivery of SCPs according to patients' information needs.

APPENDIX

CONSORT flow diagram of patient enrollment



*patients were included in the current analysis if they had no missing data on information coping style (measured at 12 months follow-up)

REFERENCES

1. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
2. Nekhlyudov L, Ganz PA, Arora NK, Rowland JH. Going Beyond Being Lost in Transition: A Decade of Progress in Cancer Survivorship. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jun 20 2017;35(18):1978-1981.
3. Jacobsen PB, DeRosa AP, Henderson TO, et al. Systematic Review of the Impact of Cancer Survivorship Care Plans on Health Outcomes and Health Care Delivery. *Journal of Clinical Oncology.*0(0):JCO.2018.2077.7482.
4. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. *Journal of Cancer Survivorship.* 2015;9(4):683-691.
5. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
6. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
7. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
8. de Rooij BH, Ezendam NPM, Nicolaije KAH, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecologic oncology.* May 2017;145(2):319-328.
9. Jefford M, Gough K, Drosdowsky A, et al. A randomized controlled trial of a nurse-led supportive care package (SurvivorCare) for survivors of colorectal cancer. *The oncologist.* 2016;21(8):1014-1023.
10. Emery JD, Jefford M, King M, et al. ProCare Trial: a phase II randomized controlled trial of shared care for follow-up of men with prostate cancer. *BJU international.* 2017;119(3):381-389.
11. Maly RC, Liang L-J, Liu Y, Griggs JJ, Ganz PA. Randomized Controlled Trial of Survivorship Care Plans Among Low-Income, Predominantly Latina Breast Cancer Survivors. *Journal of Clinical Oncology.* 2017;35(16):1814-1821.
12. Nicolaije KA, Ezendam NP, Pijnenborg JM, et al. Paper-Based Survivorship Care Plans May be Less Helpful for Cancer Patients Who Search for Disease-Related Information on the Internet: Results of the Registrationsystem Oncological Gynecology (ROGY) Care Randomized Trial. *Journal of medical Internet research.* 2016;18(7).
13. Roussi P, Miller SM. Monitoring style of coping with cancer related threats: a review of the literature. *Journal of behavioral medicine.* 2014;37(5):931-954.
14. Sweeny K, Melnyk D, Miller W, Shepperd JA. Information avoidance: Who, what, when, and why. *Review of general psychology.* 2010;14(4):340.
15. Miller SM. Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *Journal of personality and social psychology.* 1987;52(2):345.
16. Lerman C, Rimer B, Blumberg B, et al. Effects of coping style and relaxation on cancer chemotherapy side effects and emotional responses. *Cancer nursing.* 1990;13(5):308-315.
17. Miller SM, Brody DS, Summerton J. Styles of coping with threat: implications for health. *Journal of personality and social psychology.* 1988;54(1):142.
18. van Zuuren FJ, Grypdonck M, Crevits E, Walle CV, Defloor T. The effect of an information brochure on patients undergoing gastrointestinal endoscopy: a randomized controlled study. *Patient education and counseling.* 2006;64(1-3):173-182.
19. Miller SM, Mangan CE. Interacting effects of information and coping style in adapting to gynecologic stress: should the doctor tell all? *Journal of personality and social psychology.* 1983;45(1):223.
20. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2011;12:256.

21. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Factors influencing implementation of a survivorship care plan-a quantitative process evaluation of the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Aug 1 2016.
22. Netherlands Cancer Registry (NCR). *URL: http://www.cijfersoverkanker.nl/ [accessed 30-01-2015]* 2015.
23. Van Duijn C, Keij I. Sociaal-economische status indicator op postcode niveau. *Maandstatistiek van de bevolking.* 2002;50(2):32-35.
24. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: A new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003;49:156-163.
25. van Zuuren FJ, de Groot KI, Mulder NL, Peter M. Coping with medical threat: an evaluation of the Threatening Medical Situations Inventory (TMSI). *Personality and Individual Differences.* 1996;21(1):21-31.
26. Muris P, Van Zuuren F, De Jong PJ, De Beurs E, Hanewald G. Monitoring and blunting coping styles: The Miller Behavioural Style Scale and its correlates, and the development of an alternative questionnaire. *Personality and Individual Differences.* 1994;17(1):9-19.
27. Arraras JI, Greimel E, Sezer O, et al. An international validation study of the EORTC QLQ-INFO25 questionnaire: an instrument to assess the information given to cancer patients. *Eur J Cancer* 2010;46:2726-2738.
28. Bredart A, Bottomley A, Blazeby JM, et al. An international prospective study of the EORTC cancer in-patient satisfaction with care measure (EORTC IN-PATSAT32). *Eur J Cancer* 2005;41:2120-2131.
29. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res.* 2006;60:631-637.
30. Twisk JW. *Applied multilevel analysis: a practical guide for medical researchers.* Cambridge University Press; 2006.
31. Timmermans LM, van Zuuren FJ, van der Maazen RW, Leer JWH, Kraaimaat FW. Monitoring and blunting in palliative and curative radiotherapy consultations. *Psycho-Oncology: Journal of the Psychological, Social and Behavioral Dimensions of Cancer.* 2007;16(12):1111-1120.
32. Miller SM. Monitoring and blunting of threatening information: Cognitive interference and facilitation in the coping process. *Cognitive interference: Theories, methods, and findings.* 1996:175-190.
33. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Survivorship care plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients: the ROGY care trial. *Quality of Life Research.* 2018:1-12.
34. Kvale EA, Huang CS, Meneses KM, et al. Patient-centered support in the survivorship care transition: Outcomes from the Patient-Owned Survivorship Care Plan Intervention. *Cancer.* Oct 15 2016;122(20):3232-3242.
35. Jeppesen MM, Ezendam NP, Pijnenborg JM, et al. The impact of the survivorship care plan on health care use: 2-year follow-up results of the ROGY care trial. *Journal of Cancer Survivorship.* 2018;12(1):18-27.
36. Rees CE, Bath PA. Information-seeking behaviors of women with breast cancer. Paper presented at: Oncology nursing forum2001.
37. Birken SA, Urquhart R, Munoz-Plaza C, et al. Survivorship care plans: are randomized controlled trials assessing outcomes that are relevant to stakeholders? *Journal of Cancer Survivorship.* 2018:1-14.
38. American Society of Clinical Oncology (ASCO). Survivorship Care Planning Tools. *Survivorship Compendium* 2018; https://www.asco.org/practice-guidelines/cancer-care-initiatives/prevention-survivorship/survivorship-compendium. Accessed March 13, 2018, 2018.
39. Leeson SC, Beaver K, Ezendam NPM, et al. The future for follow-up of gynaecological cancer in Europe. Summary of available data and overview of ongoing trials. *European journal of obstetrics, gynecology, and reproductive biology.* Mar 2017;210:376-380.
40. de Rooij BH, Park ER, Perez GK, et al. Cluster Analysis Demonstrates the Need to Individualize Care for Cancer Survivors. *The Oncologist.* May 8, 2018 2018.

Part II: the role of illness perceptions

Chapter 5

Survivorship Care Plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients – the ROGY care trial

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ABSTRACT

Purpose: Prior results from the ROGY care trial showed that Survivorship Care Plans (SCPs) increased threatening illness perceptions in gynecological cancer survivors, but it remained unclear whether this would result in poorer physical and psychosocial outcomes. The aim of the current study is to assess the direct and indirect effects of SCPs on health-related quality of life (HRQoL) and anxiety and depression, through illness perceptions.

Methods: Twelve hospitals in the South of the Netherlands were randomized to providing 'SCP care' or 'usual care'. Newly diagnosed endometrial and ovarian cancer patients completed questionnaires after initial treatment (endometrial, 221 [75%]; ovarian, 174 [71%]) and after 6, 12 and 24 months. SCPs were automatically generated after initial treatment by the oncology providers through the web-based Registration system Oncological GYnecology (ROGY). Illness perceptions were measured after initial treatment and HRQoL and anxiety and depression after 6, 12 and 24 months.

Results: Structural equation models showed that endometrial cancer patients who experienced more symptoms or concern due to the SCP reported worse social functioning (β=-0.82; P=0.01) and more fatigue, insomnia, pain and anxiety (β=0.58-0.86, P<0.05) within 12 months after treatment. Ovarian cancer patients who had lower trust that the treatment would cure their disease due to the SCP reported worse emotional functioning 6 months after treatment (β=0.27, P=0.02).

Conclusions: Current results show that SCPs may have negative effects on HRQoL and anxiety in patients who experience more threatening illness perceptions due to the SCP. We should be aware of the potential negative consequences of SCPs.

INTRODUCTION

Over the last decade, Survivorship Care Plans (SCPs) have been recommended as a standard of care for all cancer patients. SCPs contain written information to support patients in their physical and psychological challenges in life after treatment.[1] To date, a limited number of randomized controlled trials (RCTs) have been conducted to assess the impact of SCPs on patient reported outcomes.[2-7] As opposed to observational and qualitative studies,[8,9] RCTs failed to identify beneficial effects of SCPs on patient satisfaction with information provision and care, quality of life or distress.[2-5,7,10] However, SCPs may be beneficial for underserved patient populations.[6] The Registration system Oncological GYnecology (ROGY) care trial was the first pragmatic cluster randomized controlled trial that assessed the impact of automatically generated SCPs, and did find a negative effect on illness perceptions.[5,10]

Illness perceptions are generally defined as a patient's belief about the disease through cognitive representations, including the perceived impact on life, duration of the illness, experienced symptoms and treatment trust, and also emotional representations, including concern, emotional impact and personal control over illness.[11] In the ROGY care trial, SCPs caused more threatening illness perceptions: they increased experienced symptoms, emotional impact and concern in endometrial cancer patients,[5] and led to lower trust that the treatment would help to cure the disease in ovarian cancer patients.[10]

Previous studies in cancer patients show that more threatening illness perceptions are associated with poorer quality of life and more psychological morbidities[12-18] in accordance with Leventhals' common-sense model of self-regulation (CSM). CSM presumes that individuals who are confronted with a health threat (i.e. cancer diagnosis) form illness perceptions, which impact physical and psychosocial outcomes through coping responses.[11,19] To support emotional coping, psychological interventions have been developed that aim to decrease psychological distress after an event such as a cancer diagnosis.[20] Exposure therapies, such as psychological debriefing do not seem to decrease psychological morbidity, but may even worsen it due to exacerbation of the symptoms.[21] Similarly, SCPs containing extensive information on the disease and potential side-effects may exacerbate psychological distress and symptoms experienced among cancer patients. Consequently, prior results of the ROGY care trial suggest that SCPs may intervene in the pathway of the CSM by causing more threatening illness perceptions,[5,10] which may in turn affect physical and psychosocial outcomes. However, no evidence exists on the possible causal relationships between SCP provision, illness perceptions and physical and psychosocial outcomes. It is important to consider the potential negative consequences of threatening illness perceptions due to SCPs before widespread implementation is decided upon.

The aim of the current study is to assess whether SCPs have a negative effect on long-term health-related quality of life (HRQoL), anxiety and depression in patients who experience more threatening illness perceptions due to the SCP. Illness perceptions scales that have earlier shown to be affected by SCPs[5,10] (i.e. increased experienced symptoms, concern and emotional impact in endometrial cancer, and lower treatment trust in ovarian cancer) are included in the current analysis. We hypothesize that SCPs have a negative impact on HRQoL, anxiety and depression through more threatening illness perceptions.

METHODS

Design

The ROGY care trial among endometrial and ovarian cancer patients aimed to assess the longitudinal impact of automatically generated SCPs on patient reported outcomes. A cluster-randomized design was used to avoid potential contamination between the trial arms. Twelve hospitals in the Netherlands were randomly allocated to either 'usual care' or 'SCP care'. The trial was centrally approved by a Medical Research Ethics Committee[22] and was registered as NCT01185626 in clinicaltrials.gov.

Participants and recruitment

All newly diagnosed women with endometrial cancer as a primary tumor between April 2011 and October 2012, or ovarian cancer between April 2011 and March 2014, were invited to participate shortly after initial treatment, by means of a letter and an informed consent form, sent directly to the patients' home address by their own gynecologist. After consent, questionnaires were sent after treatment and follow-up questionnaires were sent at 6, 12 and 24 months after treatment (Appendix I).

Because of the pragmatic nature of the trial, exclusion criteria (i.e. borderline ovarian tumor, undergoing palliative care or unable to complete a Dutch questionnaire) were limited [22]. Earlier analysis showed that 73% of endometrial and 66% of ovarian cancer patients in the SCP care arm reported receipt of an SCP [23]. In the current analysis, all patients of both trial arms were included (intention-to-treat) to reflect real-life clinical practice in which not all patients receive an SCP.

Randomization and blinding

To prevent imbalance between the trial arms, stratified randomization was used according to whether a hospital has a Gynecologic Oncology Center, and the annual number of endometrial and ovarian cancer patients diagnosed in each hospital. Randomization was performed via a table of random numbers, by an independent researcher blinded to the identity of the hospitals. Patients, but not oncology providers or researchers assessing the outcomes, were blinded to trial assignment.[22]

SCP care versus usual care

In 'usual care' hospitals, standard care was provided in accordance to the Dutch follow-up guidelines (www.oncoline.nl). In most hospitals, verbal information and the generic brochures of the Dutch Cancer Society were provided.[22] None of the hospitals provided SCPs as developed for this study.

In the 'SCP care' hospitals, all oncology providers (gynecologist/gynecologic oncologist and oncology nurses, N=24) attended an instruction evening devoted to when and how SCPs should be provided. They were instructed to provide an SCP to patients at the consultation where the results of histopathology and (adjuvant) treatment plan were discussed, mostly 7-14 days after surgery. If applicable (i.e. if there were any changes in the cancer, treatment or oncology provider), an updated version of the SCP could optionally be discussed in a follow-up consultation. Practical guidelines were given on the components of the SCP that should minimally be discussed with each patient during the consultation (i.e. diagnosis, prognosis, treatment(s), most important side-effects). Because of the pragmatic approach of the trial, care providers in the 'SCP care' arm were free to choose whether the gynecologist/gynecologic oncologist, or oncology nurse provided the SCP fitting their clinical practice.[22]

Survivorship care plan

The SCP was based on the Dutch translation of the American Institute of Medicine (IOM) SCP template[1], adjusted to the local situation.[22] by a group of gynecologists/gynecologic oncologists, oncology nurses, a radiotherapist, medical oncologist, primary care physician, and patients.[22] The SCP consisted of information on diagnostic tests, type of cancer, stage, grade and treatments received and contact details of the hospital and medical specialists. In addition, the SCP contained a tailored follow-up care plan, including detailed information on the most common short- and long-term effects of the treatments received, effects on social and sexual life, possible signs of recurrence and secondary tumors, and information on rehabilitation, psychosocial support, and supportive care services.[22] Texts of the SCP were based on pilot-tested patient education material from the Dutch Cancer Society. In addition, the SCP was pilot-tested on patients with a low/intermediate educational level to ensure that the SCP was understandable.

Measures

Age, socio-economic status (SES) and clinical data, such as cancer type, cancer stage and date of diagnosis, were obtained from the Netherlands Cancer Registry (NCR). The NCR routinely collects data on newly diagnosed cancer patients in all hospitals in the Netherlands.[24] SES was based on postal code of the residence area of the patient, combining aggregated individual fiscal data on the economic value of the home and household incomes.[25] SES was categorized into low, medium or high. Additional socio-

demographic information (i.e. marital status, employment status and comorbidities) was assessed in the first questionnaire. Marital status ('married/living together' versus 'divorced/widowed/never married') and employment status ('having a paid job' versus 'not having a paid job') were dichotomized. Comorbidity was assessed by the adapted Self-administered Comorbidity Questionnaire (SCQ), and categorized into no comorbidities, one comorbidity or more than one comorbidity.[26]

The Brief Illness Perception Questionnaire (B-IPQ) was used to assess illness perceptions after initial treatment.[27] The B-IPQ includes eight single-item scales (impact of disease on life, perceived duration of illness, personal control over illness, trust that the treatment would help to cure the illness, experienced symptoms, concern about the illness, understanding of the illness and emotional impact of the illness).Only the scales that have earlier shown to be affected by SCPs in our trial [5,10] were used in the analysis, including the amount of symptoms experienced, concerns about the illness, emotional impact of the illness with respect to endometrial cancer, and trust that the treatment would help to cure with respect to ovarian cancer.[28] The latter scale was reversed to ascertain that all B-IPQ scales were one-directional: a higher score indicates more threatening illness perceptions. Test-retest reliability (Pearson correlations 0.42-0.75) was fair.[27]

The EORTC QLQ-C30 (version 3.0) was used to assess HRQoL 6, 12 and 24 months after diagnosis.[29] It contains five functional scales on physical, role, cognitive, emotional and social functioning, a global QoL scale, three symptom scales on fatigue, nausea and vomiting, and pain, and six single items. Response scales included: 'Not at all', 'A bit', 'Quite a bit', and 'Very much', except for the global QoL scale, which ranges from 'Very poor' to 'Excellent'. Latent variables of the scales were defined by the items of each scale.[30] Higher scores on global quality of life and the function scales indicate a better HRQoL, while higher scores on the symptom scales indicate more symptoms. Test-retest reliability was good (Pearson correlations=0.82-0.91).[31] Internal consistency of the multi-item scales (Cronbach's alphas 0.71-0.92) in our study was good.

The Hospital Anxiety and Depression Scale (HADS) was used to assess symptoms of anxiety and depression 6, 12 and 24 months after diagnosis.[32] The HADS assesses separate anxiety and depression scales, which both consist of 7 items. All items were scored on a 0 to 3-point scale, with higher scores indicating more symptoms. Test-retest reliability of the scales (Pearson correlations=0.86-0.88) was good.[32] Internal consistency of the scales (Crohnbach's alphas 0.71-0.77) in our study was good.

Statistical Analysis

Statistical analyses were conducted using Statistical Analysis System (SAS) version 9.4. (SAS Institute, Cary, NC, 1999). Differences in characteristics of patients between the trial arms

for endometrial and ovarian cancer were compared using independent samples t-tests for normally distributed continuous variables, Mann-Whitney U-tests for not normally distributed variables and chi-square tests for categorical variables. Differences in baseline B-IPQ scores between the trial arms were assessed using chi-square tests of categorical variables defined by the 25th, 50th, 75th and 100th percentile scores of the separate B-IPQ scales.

Pearson's correlation coefficients were computed to assess the correlations between the illness perception scales at baseline and outcomes (HRQoL, anxiety and depression) 6, 12, and 24 months after initial treatment, for endometrial and ovarian cancer separately. P-values smaller than .05 were considered to be statistically significant.

Structural equation models (SEM) were used to test the hypothesized causal relationships between trial allocation (SCPs), illness perceptions and the HRQoL, and anxiety and depression scales, with a linear equation system. SEMs are used to assess unobservable 'latent' variables by using observed variables, and to assess the relationships between those (observed and latent) variables.[33] Both direct and indirect effects of trial allocation on outcome variables were assessed using the *effpart* statement in the *CALIS procedure* in SAS. Direct effects would indicate an effect of SCPs on the outcome scales in all patients, while indirect effects would indicate an effect of SCPs on the outcome scales in patients who have altered illness perceptions due to the SCP. Statistical power was sufficient to detect indirect effects, but low to detect direct effects.[34] The CALIS procedure was used to define the model paths (i.e. hypothesized relationships between variables). First, simple mediation models were built to assess the direct and indirect effects of trial allocation on the separate outcome scales (HRQoL, anxiety and depression scales) 6, 12 and 24 months after initial treatment. Mediators were the separate BIPQ scales measured after initial treatment that have earlier shown to be associated with trial allocation (i.e. increased experienced symptoms, concern and emotional impact in endometrial cancer, and lower treatment trust in ovarian cancer; Fig 1). Models were defined for endometrial and ovarian cancer separately. The paths in each simple mediation model were defined as: *trial allocation* ---> [*BIPQ item score after diagnosis*] ---> [*outcome variable at time-point X*]. When outcome scales consisted of multiple items, a latent variable was defined by the items of that scale. When standardized factor loadings of scale items were low ($\beta<0.6$), they were removed from the model to obtain a better model fit.[35] When (semi-)complete separation of the outcome scales occurred, no SEM could be determined.[36] Second, the full SEMs were built by entering all significant paths ($P<0.05$) of the simple mediation models into one model, for endometrial and ovarian separately, and for each time-point separately. Third, the insignificant paths ($p>0.05$) were removed from the model to obtain a good model fit. Finally, the covariates that were significantly associated with any of the outcome scales were entered into the model. For all SEM models, full information

maximum likelihood (FIML) was used, which handles missing data within the model without needing to impute data.[37] Model fit was assessed with the chi^2 statistic, adjusted goodness-of-fit-index (AGFI), Bentler's comparative fit index (CFI), standardized root mean squared residual (SRMR) and root mean squared error approximation (RMSEA).[38] Standardized beta coefficients were used to interpret the models, and range from -1 to 1, in which coefficients closer to zero indicate smaller effects. An increase of 1 standard deviation of the independent variable corresponds to an increase in standard deviation of the dependent variable by the standardized beta coefficient.[39] Standardized beta coefficients of indirect effects can be considered small (0.05-0.10), moderate (0.1-0.25) or large (>0.25).[39]

RESULTS

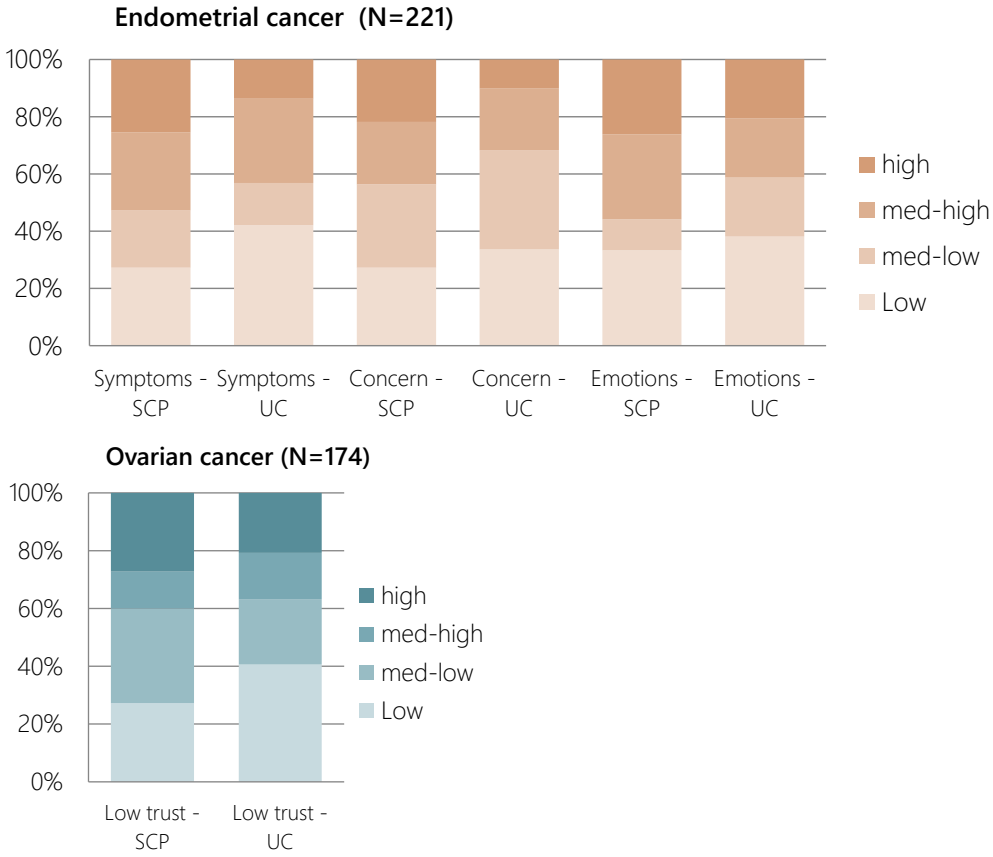
Table 1 shows the clinical and socio-demographic baseline characteristics for both endometrial and ovarian cancer patients in the SCP care and usual care conditions. In endometrial cancer, patients in the 'SCP care' took more time after diagnosis to complete the questionnaires than patients in the 'Usual care' arm ($p<0.01$). No differences in baseline characteristics were found between the trial arms in ovarian cancer patients.

Figure 1 shows the differences in illness perceptions between the SCP care and usual care arms. Significantly more endometrial patients in the SCP care arm compared to the usual care arm reported high experienced symptoms (18% vs. 9%, $p=0.02$) and high concerns about the illness (16% vs. 7%, $p=0.02$). No significant differences between the trial arms were found in emotional impact of the disease (19% vs. 14%, $p=0.27$) in endometrial cancer, or low trust that the treatment would help to cure the illness (16% vs. 14%, $p=0.60$) in ovarian cancer. However in earlier multilevel linear mixed model analyses, SCPs significantly increased threatening illness perceptions on these scales.[5,10]

Table 1: baseline clinical and socio-demographic characteristics endometrial and ovarian cancer patients, SCP care versus usual care

	ENDOMETRIAL CANCER			OVARIAN CANCER		
	SCP care (N=119)	Usual care (N=102)	P-value	SCP Care (n=61)	Usual Care (n=113)	p-value*
Age at survey						
Mean (SD)	67.4 (9.1)	67.8 (8.9)	0.71	63.6 (11.2)	64.3 (10.7)	0.67
SES[a], n (%)						
High	43 (36)	36 (35)	0.60	25 (41)	44 (39)	0.12
Intermediate	49 (41)	42 (41)		15 (25)	44 (39)	
Low	21 (18)	22 (22)		12 (20)	18 (16)	
Unknown	6 (5)	2 (2)		9 (15)	7 (6)	
Months since diagnosis, n(%)						
Median	2.2	1.5	<0.01	3.0	2.4	0.31
<1	12 (10)	24 (24)		8 (13)	26 (23)	
1-2	40 (34)	46 (45)		18 (30)	39 (34)	
2-3	33 (28)	20 (20)		8 (13)	17 (15)	
>3	34 (29)	12 (12)		27 (44)	32 (28)	
Comorbidity, n(%)						
None	19 (16)	18 (18)	0.53	21 (34)	28 (25)	0.18
1	32 (27)	20 (20)		12 (20)	36 (32)	
2 or more	64 (54)	62 (61)		26 (43)	48 (36)	
Unknown	4 (3)	2 (2)		2 (3)	8 (7)	
Marital status[b], n(%)						
Partner	85 (71)	76 (75)	0.74	48 (79)	82 (73)	0.39
No partner	31 (26)	25 (25)		13 (21)	31 (27)	
Unknown	3 (3)	1 (1)		0 (0)	0 (0)	
Employed, n (%)						
Yes	22 (18)	15 (15)	0.40	20 (33)	31 (27)	0.44
No	85 (71)	79 (77)		41 (67)	83 (73)	
Unknown	12 (10)	8 (8)		0 (0)	0 (0)	
FIGO-stage, n (%)						
I	102 (85)	89 (87)	0.34	21 (34)	31 (27)	0.63
II	6 (5)	1 (1)		7 (11)	9 (8)	
II	9 (8)	9 (8)		23 (38)	50 (44)	
IV	2 (2)	3 (3)		10 (16)	20 (18)	
Unknown	0 (0)	0 (0)		0 (0)	3 (3)	
Treatment, n (%)						
Surgery	117 (99)	97 (98)	0.46	54 (88)	104 (93)	0.33
Chemotherapy	6 (5)	12 (12)	0.06	44 (72)	92 (82)	0.13
Radiotherapy	44 (37)	37 (37)	0.99			

[a]Socio-economic status (SES) was based on postal code of the residence area of the patient. [b]Marital status included: partner = married/living together; no partner = divorced/widowed/never married. The numbers may not always add up to 100, because percentages have been rounded off to whole numbers.



Note: Only the illness perception items were included that have earlier been associated with trial allocation. High, med-high, med-low, and low illness perception categories were defined by the 25th, 50th, 75th and 100th percentile scores of each B-IPQ scale separately

Figure 1: Bar charts of illness perceptions after diagnosis, SCP care (SCP) versus Usual Care (UC)

Table 2 shows the correlations between illness perception scales after diagnosis and HRQoL, anxiety and depression after 6, 12 and 24 months, corrected for multiple testing (Bonferroni correction, $\alpha<0.003$). Consistent with our hypothesis, in both endometrial and ovarian cancer, significant moderate negative Pearson's correlations were found between B-IPQ items and functioning scales ($r= -0.25$ to -0.41, $p<0.003$). Significant moderate positive Pearson's correlations were found between B-IPQ items and symptom scales ($r=0.27 – 0.41$, $p<0.003$), and between B-IPQ scales and anxiety and depression ($r= 0.28 – 0.46$, $p<0.003$).

Table 2: Correlations between illness perception scales after diagnosis and HRQoL, anxiety and depression after 6, 12 and 24 months

	ENDOMETRIAL CANCER									OVARIAN CANCER		
Illness perceptions after treatment	Symptoms experienced			Concerns			Emotional impact			Lower treatment trust		
Months after treatment, outcome variables	6	18	24	6	18	24	6	18	24	6	18	24
N	158	147	128	158	147	128	158	147	128	124	101	75
Global quality of life	-0.24	**-0.25***	-0.21	**-0.25***	**-0.29***	**-0.34***	**-0.29***	**-0.29***	**-0.29***	**-0.42***	**-0.40***	**-0.36***
Function scales												
Physical Functioning	-0.22	-0.19	-0.24	-0.14	-0.21	-0.19	-0.18	-0.22	-0.18	-0.24	-0.16	-0.16
Role Functioning	-0.06	-0.20	**-0.28***	-0.09	-0.15	**-0.36***	-0.22	-0.13	-0.25	-0.27	-0.18	-0.25
Emotional functioning	**-0.34***	-0.21	**-0.32***	**-0.32***	-0.24	**-0.38***	**-0.38***	**-0.29***	**-0.41***	**-0.28***	-0.15	-0.27
Cognitive functioning	-0.17	-0.07	-0.25	-0.14	-0.17	**-0.28***	-0.17	-0.06	-0.22	-0.19	-0.29	-0.34
Social functioning	**-0.41***	**-0.28***	**-0.32***	-0.23	**-0.29***	**-0.38***	**-0.33***	**-0.27***	**-0.27***	-0.16	-0.07	-0.26
Symptom scales												
Fatigue	**0.36***	**0.28***	**0.34***	0.26	0.26	0.37	**0.35***	**0.31***	**0.32***	0.26	0.14	0.29
Nausea and vomiting	0.13	0.21	0.24	0.06	0.05	0.14	0.15	0.09	0.12	0.14	0.15	0.33
Pain	0.23	0.17	0.26	0.20	0.23	**0.39***	0.22	0.20	0.26	**0.28***	0.19	0.33
Dyspnea	0.18	0.19	0.11	0.07	0.14	0.14	0.15	0.15	0.20	0.20	0.02	0.23
Insomnia	**0.32***	0.17	0.25	0.23	0.19*	**0.28***	**0.30***	0.22	0.26	**0.31***	0.20	0.18
Appetite loss	**0.28***	0.16	0.23	0.18	0.03	**0.28***	**0.27***	0.14	0.24	0.22	0.09	**0.44***
Constipation	0.04	0.03	0.09	0.11	0.02	0.22	0.14	0.08	0.22	0.21	0.21	0.14
Diarrhea	0.18	0.11	0.13	0.15	0.11	0.05	0.21	0.08	0.14	0.06	<0.01	0.13
Financial difficulties	**0.30***	**0.20***	0.20	0.17	0.08	0.11	0.21	0.10	0.08	0.16	0.09	-0.08
Anxiety	**0.30***	**0.33***	**0.34***	**0.41***	**0.45***	**0.46***	**0.46***	**0.47***	**0.45***	**0.39***	0.31	0.24
Depression	**0.39***	**0.28***	**0.23***	**0.35***	**0.35***	**0.36***	**0.39***	**0.33***	**0.34***	**0.40***	0.25	**0.38***

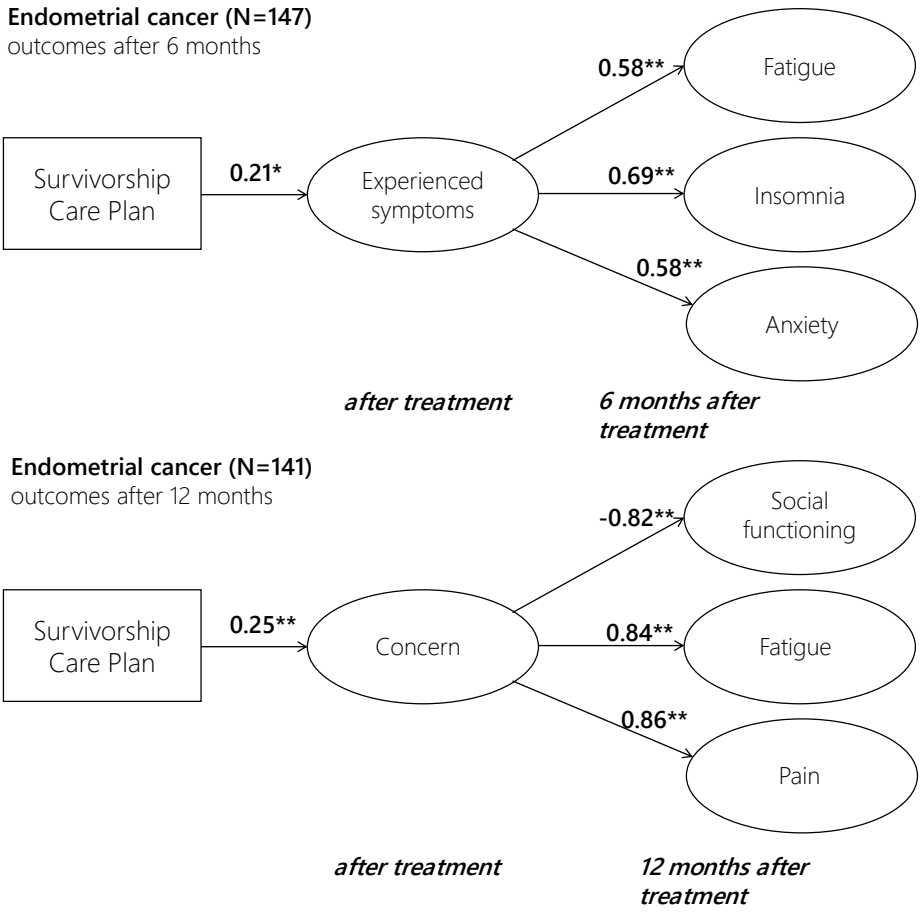
Note: Pearson's correlations were estimated between illness perceptions measured after diagnosis, and outcome variables after diagnosis and 6, 12 and 24 months after diagnosis. Only the illness perception items were included that have earlier been associated with trial allocation. *p<0.003 (adjusted for Bonferroni correction 0.05/1

The SEM models showed no direct effects of SCPs on HRQoL, anxiety and depression scales. However, indirect effects trough illness perceptions were observed. In endometrial cancer, SCPs indirectly increased fatigue, insomnia and anxiety after 6 months (standardized, β=0.58, SE=0.09, p<0.01; β=0.69, SE=0.08, p<0.01; β=0.58, SE=0.09, P=0.01), through more experienced symptoms (standardized, β=0.21, SE=0.09, p=0.02; Fig 2). Model fit was reasonable to good (AGFI=0.87; CFI=0.93; SRMR=0.07; RMSEA=0.047 [95% CI=0.03-0.06]; Chi^2=87.2, P<0.01) and effect sizes of the indirect effects are moderate (standardized, β=0.12, SE=0.06, p=0.03; β=0.15, SE=0.06, p=0.02; β=0.12, SE=0.05, p=0.03).[39] Further, SCPs indirectly decreased social functioning after 12 months (standardized, β=-0.82, SE=0.06, p<0.01), and increased fatigue and pain after 12 months (standardized, β=0.84, SE=0.05, p<0.01; β=0.86, SE=0.05, p<0.01), through more concern (standardized, β=0.25, SE=0.09, p<0.01;Fig 2). Model fit was good (AGFI=0.90; CFI=0.98; SRMR=0.046; RMSEA=0.04 [95% CI=0.00-0.06]; Chi^2=34.4, P=0.08) and the effect sizes of the indirect effects were moderate (standardized, β=- 0.20, SE=0.07, p<0.01; β= 0.21, SE=0.07, P<0.01; β= 0.22, SE=0.08, p<0.01)[39]. In ovarian cancer, SCPs indirectly decreased emotional functioning after 6 months (standardized, β=-0.66, SE=0.20 p<0.01), through lower trust that the treatment would help to cure the disease (standardized, β=0.27, SE=0.12, p<0.05) (Fig 2). Model fit was good (AGFI=0.90; CFI=0.96; SRMR=0.06; RMSEA=0.06 [95% CI=0.01-0.09]; Chi^2=23.1, P=0.04), and the effect size of the indirect effect was moderate (standardized, β=- 0.18, SE=0.08, p=0.02)[39]. No significant paths in the simple mediation models were found for outcomes after 24 months, for both endometrial and ovarian cancer.

DISCUSSION

The current study among endometrial and ovarian cancer patients shows that SCPs have a negative impact on long-term HRQoL and anxiety in patients who experience more threatening illness perceptions due to the SCP. Endometrial cancer patients who experience more symptoms or concerns due to the SCP, report worse social functioning and more fatigue, insomnia, pain and anxiety in the year following treatment. Ovarian cancer patients who have lower trust that the treatment would cure their disease due to the SCP report worse emotional functioning 6 months after initial treatment.

Earlier findings from the ROGY Care trial already showed that SCPs increased threatening illness perceptions: higher experienced symptoms, concern and emotional impact in endometrial cancer patients, and decreased trust that the treatment would help to cure the disease in ovarian cancer patients.[5,10] However, it was yet unclear whether these threatening illness perceptions would deteriorate long-term physical and psychosocial outcomes. Our study confirms earlier findings in cancer patients that more threatening illness perceptions are associated with worse physical and psychosocial outcomes.[12-18] Consequently, our analyses confirmed that threatening illness perceptions due to the



Note: only the significant paths between the intervention (SCP), illness perception items, and outcome scales were entered in this model to obtain good model fit. Standardized coefficients are shown. Standardized beta coefficients were used to interpret the models, and range from -1 to 1, in which coefficients closer to zero indicate smaller effects. Error terms and covariates in the model (age, FIGO stage, number of comorbidities) have been removed from the figure. *P<0.05, **P<0.01.

Figure 2: path diagrams of the final structural equation models, outcomes 6 and 12 months after treatment

SCP led to worse HRQoL and more anxiety. Although no direct effects of SCPs were found, our results support our hypothesis that SCPs have a negative impact on HRQoL and anxiety through more threatening illness perceptions, consistent with Leventhal's CSM.[11]Illness perceptions that mediated between SCP provision and HRQoL and anxiety were experienced symptoms and concern in endometrial cancer, and low treatment trust in ovarian cancer patients. Possibly, endometrial cancer patients, who are often diagnosed with low cancer stages, may perceive their cancer as a more serious condition due to information provided in the SCP (i.e. the diagnosis and treatments received, possible long-term and late effects, and chance of recurrence) than would otherwise be communicated by the oncology provider. The overall perception of a more serious condition in endometrial cancer patients may have caused higher symptom awareness, more anxiety and the belief that one is unable to participate in social activities.[17] In ovarian cancer patients, who are more often diagnosed at advanced stages, the SCP led to lower treatment trust, possibly due to information on chance of recurrence in the SCP. Although this information may be realistic, it led to decreased emotional functioning after 6 months, meaning that patients felt more tense, worried, irritable or depressed. Indeed, fear of recurrence has earlier been found to be most strongly associated with emotional functioning, of all EORTC QLQ-C30 functioning scales.[40]

A limitation of the current study is that not all patients in the SCP arm reported receipt of an SCP.[23] A process evaluation of the ROGY Care Trial showed that ovarian cancer patients, older patients and patients who have a distressed (type D) personality less often received an SCP.[23] We performed intention-to-treat analysis to reflect real-life clinical practice in which not all patients receive an SCP. Therefore, our results possibly underestimate the effects of SCPs on HRQoL, anxiety and depression in the total population, as patients with a type D personality may be more likely to experience threatening illness perceptions due to the SCP.[41] Further, as shown earlier,[10] ovarian cancer patients with higher cancer stages were more often lost to follow-up due to death or ill-health, and were therefore not included in our longitudinal analyses. Therefore, current results in ovarian cancer may represent the healthier patient with lower cancer stages. However, we aimed to minimize selection bias by limiting exclusion criteria and our response rates were relatively high.

Our SEM analyses violated the well-known recommendation of Baron and Kenny's (1986) that a significant relationship between the independent variable (SCPs) and outcome (HRQoL, anxiety and depression) is required, in order to evaluate mediation effects.[42] However, this recommendation has since been criticized.[34,43] Kenny and Judd (2014) argued that sample sizes needed to detect direct effects between independent and dependent variables, should be much larger than to detect indirect effects through mediation.[34] Therefore, our sample sizes of endometrial and ovarian cancer separately, were too small to detect direct effects of SCPs on the outcome scales. Possibly, direct effects of SCPs on

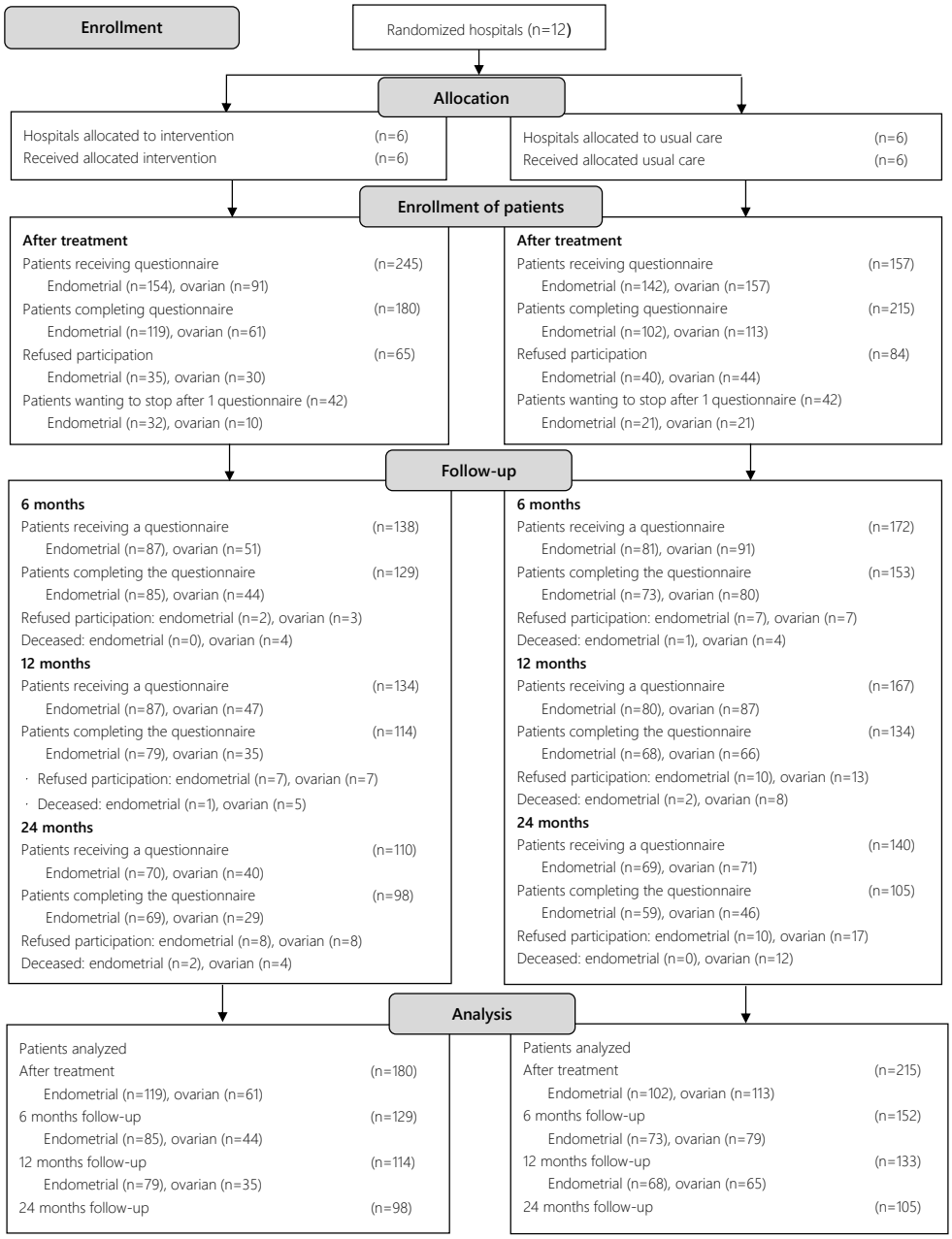
the outcome scales would be found in larger sample sizes. An alternative explanation of our findings is the presence of a suppressing mediator, such as coping, which may ameliorate the indirect impact of SCPs on physical and psychological outcomes, while at the same time illness perceptions deteriorate the indirect impact of SCPs on outcomes. Therefore, there may be indirect effects but no direct effects of SCPs on HRQoL and anxiety,[43] which would indicate that the impact of SCPs works differently across coping styles.

In earlier studies of the ROGY care trial,[5,10] we argued that information provided in an SCP could be perceived as threatening but may also be *realistic*. Providing patients with honest and realistic information may be considered best to prepare patients for potential consequences of the cancer and cancer treatments, or would encourage patients to find social support to cope with the disease.[44] However, the current study shows that realistic information is not self-evidently beneficial for all patients. Instead, patients may attain worse expectations about negative outcomes such as side-effects or a recurrence, which has shown to potentially cause clinical worsening ("nocebo effect").[45] Similarly, psychological interventions that expose individuals to facts and rethinking of an event (i.e. cancer diagnosis and treatments) may not necessarily decrease psychological distress but rather exacerbate symptoms.[21] Possibly, patients with certain personality types or coping styles may be more vulnerable to the harmful effects of exposure interventions such as SCPs. On the other hand, one may argue that patients benefit from having received realistic information on the chance of recurrence in an SCP, after they eventually develop a recurrence. Little is known about the effect of exposure to information about a potentially negative outcome, after the negative outcome has manifested. Unfortunately, numbers of patients with a recurrence in our trial were too small to investigate the impact of SCPs in these patients after diagnosis of a recurrence. Further moderation analysis considering patient characteristics, personality and coping could further reveal which patients do, and which patients do not benefit from SCPs.

In conclusion, no beneficial effects of SCPs on satisfaction with information provision and care in both endometrial and ovarian cancer patients were shown as primary outcomes of our trial.[5,10] The current study highlights that SCPs may even have negative effects on HRQoL and anxiety in patients who experience more threatening illness perceptions due to the SCP. Therefore, we should be aware of the potential negative consequences of SCPs in some patients. A more tailored approach such as personalized SCPs fitting individual patient's information needs should be further explored.

APPENDIX

CONSORT flow-diagram of endometrial and ovarian cancer patient enrollment



REFERENCES

1. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
2. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
3. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
4. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment.* 2013;138(3):795-806.
5. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
6. Maly RC, Liang L-J, Liu Y, Griggs JJ, Ganz PA. Randomized Controlled Trial of Survivorship Care Plans Among Low-Income, Predominantly Latina Breast Cancer Survivors. *Journal of Clinical Oncology.* 2017;35(16):1814-1821.
7. de Rooij BH, Ezendam NPM, Nicolaije KAH, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecologic oncology.* May 2017;145(2):319-328.
8. Brennan M, Gormally J, Butow P, Boyle F, Spillane A. Survivorship care plans in cancer: a systematic review of care plan outcomes. *British journal of cancer.* 2014;111(10):1899-1908.
9. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
10. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up – the ROGY Care trial. *Gynecologic Oncology (in press).* 2017.
11. Leventhal H, Leventhal EA, Contrada RJ. Self-regulation, health, and behavior: A perceptual-cognitive approach. *Psychology and Health.* 1998;13(4):717-733.
12. Ashley L, Marti J, Jones H, Velikova G, Wright P. Illness perceptions within 6 months of cancer diagnosis are an independent prospective predictor of health-related quality of life 15 months post-diagnosis. *Psycho-oncology.* Nov 2015;24(11):1463-1470.
13. Gray NM, Hall SJ, Browne S, et al. Modifiable and fixed factors predicting quality of life in people with colorectal cancer. *British journal of cancer.* May 24 2011;104(11):1697-1703.
14. Hopman P, Rijken M. Illness perceptions of cancer patients: relationships with illness characteristics and coping. *Psycho-oncology.* Jan 2015;24(1):11-18.
15. Keeling M, Bambrough J, Simpson J. Depression, anxiety and positive affect in people diagnosed with low-grade tumours: the role of illness perceptions. *Psycho-oncology.* Jun 2013;22(6):1421-1427.
16. Millar K, Purushotham AD, McLatchie E, George WD, Murray GD. A 1-year prospective study of individual variation in distress, and illness perceptions, after treatment for breast cancer. *Journal of psychosomatic research.* Apr 2005;58(4):335-342.
17. Rozema H, Vollink T, Lechner L. The role of illness representations in coping and health of patients treated for breast cancer. *Psycho-oncology.* Aug 2009;18(8):849-857.
18. Traeger L, Penedo FJ, Gonzalez JS, et al. Illness perceptions and emotional well-being in men treated for localized prostate cancer. *Journal of psychosomatic research.* Nov 2009;67(5):389-397.
19. Leventhal H, Meyer D, Nerenz D. The common sense representation of illness danger. *Contributions to medical psychology.* 1980;2:7-30.
20. Andersen BL. Psychological interventions for cancer patients to enhance the quality of life. *Journal of consulting and clinical psychology.* 1992;60(4):552.

21. Rose SC, Bisson J, Churchill R, Wessely S. Psychological debriefing for preventing post traumatic stress disorder (PTSD). *The Cochrane Library.* 2002.
22. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials.* 2011;12:256.
23. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Factors influencing implementation of a survivorship care plan-a quantitative process evaluation of the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Aug 1 2016.
24. NKR NCR. Netherlands Cancer Registration *URL: http://www.cijfersoverkanker.nl/ [accessed 30-01-2015]* 2015.
25. Van Duijn C, Keij I. Sociaal-economische status indicator op postcode niveau. *Maandstatistiek van de bevolking.* 2002;50(2):32-35.
26. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: A new method to assess comorbidity for clinical and health services research. *Arthritis Rheum* 2003;49:156-163.
27. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res.* 2006;60:631-637.
28. de Raaij EJ, Schröder C, Maissan FJ, Pool JJ, Wittink H. Cross-cultural adaptation and measurement properties of the Brief Illness Perception Questionnaire-Dutch Language Version. *Man Ther.* 8// 2012;17(4):330-335.
29. Niezgoda HE, Pater J. A validation study of the domains of the core EORTC quality of life questionnaire. *Quality of Life Research.* 1993;2(5):319-325.
30. Fayers P, Aarson N, Bjordal K, Sullivan M. QLQ C-30 scoring manual/EORTC Study Group on Quality of Life. Brussels; 1995.
31. Hjermstad MJ, Fossa SD, Bjordal K, Kaasa S. Test/retest study of the European Organization for Research and Treatment of Cancer Core Quality-of-Life Questionnaire. *Journal of Clinical Oncology.* 1995;13(5):1249-1254.
32. Spinhoven P, Ormel J, Sloekers PP, Kempen GI, Speckens AE, Van Hemert AM. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological medicine.* Mar 1997;27(2):363-370.
33. Kline RB. *Principles and practice of structural equation modeling.* 3rd ed. New York: Guilford Press; 2011.
34. Kenny DA, Judd CM. Power anomalies in testing mediation. *Psychological Science.* 2014;25(2):334-339.
35. Guadagnoli E, Velicer WF. Relation to sample size to the stability of component patterns. *Psychological bulletin.* 1988;103(2):265.
36. Allison P, Altman M, Gill J, McDonald MP. Convergence problems in logistic regression. *Numerical issues in statistical computing for the social scientist.* 2004:238-252.
37. Muthén B, Kaplan D, Hollis M. On structural equation modeling with data that are not missing completely at random. *Psychometrika.* 1987;52(3):431-462.
38. Hooper D, Coughlan J, Mullen M. Structural equation modelling: Guidelines for determining model fit. *Articles.* 2008:2.
39. Keith TZ. *Multiple regression and beyond: An introduction to multiple regression and structural equation modeling.* Routledge; 2014.
40. Wal M, Poll-Franse L, Prins J, Gielissen M. Does fear of cancer recurrence differ between cancer types? A study from the population-based PROFILES registry. *Psycho-Oncology.* 2015.
41. Mols F, Denollet J, Kaptein AA, Reemst PH, Thong MS. The association between Type D personality and illness perceptions in colorectal cancer survivors: a study from the population-based PROFILES registry. *Journal of psychosomatic research.* 2012;73(3):232-239.
42. Baron RM, Kenny DA. The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations. *Journal of personality and social psychology.* 1986;51(6):1173.
43. Cerin E, MacKinnon DP. A commentary on current practice in mediating variable analyses in behavioural nutrition and physical activity. *Public health nutrition.* 2009;12(08):1182-1188.

44. Walshe C, Roberts D, Appleton L, et al. Coping Well with Advanced Cancer: A Serial Qualitative Interview Study with Patients and Family Carers. *PloS one*. 2017;12(1):e0169071.
45. Benedetti F, Lanotte M, Lopiano L, Colloca L. When words are painful: unraveling the mechanisms of the nocebo effect. *Neuroscience*. 2007;147(2):260-271.

6

Chapter 6

Optimistic, realistic and pessimistic illness perceptions, quality of life and survival among 2457 cancer survivors: the population-based PROFILES registry

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ABSTRACT

Background: Threatening illness perceptions (IPs) have been associated with poorer health outcomes. However, to the authors' knowledge, it remains unclear whether threatening IPs that are consistent with disease severity are equally harmful. The aim of the current study is to 1) identify subgroups of cancer survivors based on IPs and prognosis, and 2) assess health-related quality of life (HRQoL) and survival associated with these subgroups.

Methods: The authors used survey data from the population-based PROFILES registry, which were collected between 2008 and 2015 and included 2,457 cancer survivors who were <5 years after their cancer diagnosis (colon, rectal, prostate, endometrial, ovarian, or non-Hodgkin lymphoma). Clinical and survival data were collected through the Netherlands Cancer Registry. Subgroups were defined by IP (Brief Illness Perceptions Questionnaire) and prognosis (conditional 5-year relative survival) into survivors with a) IP consistent with prognosis ('realistic'), b) less threatening IP than expected based on prognosis ('optimistic'), and c) more threatening IP than expected based on prognosis ('pessimistic').

Findings: Compared to survivors with realistic IPs (1230 survivors), those with optimistic IPs (582 survivors) were found to have a higher HRQoL ($p<.01$ on all European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 [EORTC QLQ-C30] scales), and a lower all-cause mortality (hazard ratio, 0.72; $p<.01$), whereas those with pessimistic IPs (N=645) had a lower HRQoL ($p<0.01$ on all scales) and a higher all-cause mortality (hazard ratio, 1.52; $p<0.01$).

Conclusions: Optimistic IPs are associated with a better HRQoL and survival, even if they may appear to be unrealistic with respect to cancer survivors' prognosis. Survivors with pessimistic IPs appear to have the worst outcomes. Therefore, efforts are needed to provide better support to patients with pessimistic IP to improve their outcomes.

INTRODUCTION

The illness perceptions (IPs) of patients, comprising both cognitive and emotional responses to their illness, are increasingly studied in relation to physical and psychological outcomes.[1] Threatening IPs, such as concern about the disease and the number of symptoms experienced, have been associated with poor health-related quality of life (HRQoL), psychological morbidities, and low survival among cancer survivors.[2-10] These findings suggest that having threatening IPs affect survivors' outcomes. However, IPs may accurately reflect a patients' true disease status, indicating that the associations between IP and outcomes largely are explained by disease severity (i.e., prognosis).[4] Conversely, patients also could hold more optimistic or pessimistic beliefs of the disease that are not consistent with disease severity or prognosis.

The IPs of cancer survivors may become more concordant with disease severity or prognosis when these individuals receive explicit information regarding the diagnosis, side effects, and prognosis of their cancer.[11-13] In patients with cancer who are receiving palliative care, realistic perceptions of prognosis may contribute to acceptance of the disease and its consequences, without being disappointed or frustrated with unachievable expectations.[14-16] However, to the best of our knowledge, the advantages of realistic IPs among cancer survivors remain unclear. Efforts to investigate the benefits of realistic, pessimistic or optimistic IPs relative to prognosis among cancer survivors may provide insights into survivors' perspectives, and may provide information with which to guide information provision and support to those at risk of physical and emotional symptoms.

In a large observational cohort of cancer survivors with various cancer diagnoses, we sought to identify subgroups of survivors with realistic, pessimistic or optimistic IPs relative to prognosis at the time of the questionnaire. In addition, we aimed to assess the HRQoL and survival associated with these subgroups. In parallel with literature demonstrating the benefits of prognostic awareness in patients receiving palliative care,[14,15] we hypothesized that realistic IPs among cancer survivors are associated with better outcomes compared with either optimistic or pessimistic IPs.

METHODS

Design/setting

We used data from the PROFILES ('Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship') registry.[17] Patient-reported outcomes are collected within a sampling frame of the Netherlands Cancer Registry (NCR) and can be linked with clinical data of all individuals newly diagnosed with cancer in the Netherlands.

Data collection

A detailed description of the data-collection has been presented previously.[17] In brief, in each study sample, cancer survivors were informed about the study via a letter from their attending specialist. This letter contained either an informed consent form and a paper questionnaire, or a secured link to a Web-based informed consent form and online questionnaire. In study samples in which the secured link was provided, the patient could return a postcard to request a paper-and-pencil questionnaire if preferred. Data from the PROFILES registry are freely available for non-commercial scientific research, subject to study question, privacy and confidentiality restrictions, and registration (www.profilesregistry.nl).

Study population

The current analysis included 5 study samples from the PROFILES registry for which data were available regarding dependent and independent variables. Only short-term cancer survivors (<5 years after diagnosis) were included, because, among long-term cancer survivors, the IP may be less likely to be related to the cancer diagnosis and more likely the consequence of comorbid conditions. Cancer types included colon, rectal, prostate, endometrial, and ovarian cancer as well as non-Hodgkin lymphoma. In all study samples, a core set of the same questionnaires was used, with inclusion between May 2009 and March 2014. Participants were excluded if they were not able to complete a Dutch questionnaire according to their (ex-)attending specialist (ie, due to cognitive impairment, being a non-native speaker, being too ill to participate). Also excluded were individuals who died or emigrated before the initiation of the study, according to data from the hospital of diagnosis and/or data from the Dutch municipal personal records database (ie, mortality and residential data from all citizens through municipal registries). Ethical approval was obtained for all study samples separately from a local certified medical ethics committee.

Measures

Clinical data, such as the date of diagnosis, tumor type, tumor stage, and primary treatments received were obtained from the NCR. The NCR routinely collects data concerning newly diagnosed patients with cancer in all hospitals in the Netherlands. Tumor type was classified according to the *International Classification of Diseases for*

Oncology, 3rd Edition (ICD-O-3),[18] and cancer stage was classified according to TNM[19] or Ann Arbor Code (Non-Hodgkin lymphoma). Primary treatments received were classified as surgery, systemic therapy (chemotherapy, targeted therapy, immune therapy), radiotherapy (including brachytherapy), hormone therapy, no treatment/active surveillance or unknown. The time from diagnosis at time of questionnaire invitation was categorized into quartiles (0-2 years, 2-3 years 3-5 years and >5 years). Sociodemographic information (i.e. education, marital status, employment status and comorbidity) was assessed in the questionnaire. Marital status ('married/living together' versus 'divorced/widowed/never married') and employment status ('having a paid job' versus 'not having a paid job') were dichotomized. Comorbidity was assessed using the adapted Self-administered Comorbidity Questionnaire (SCQ), and categorized into no comorbidities, one comorbidity or more than one comorbidities.[20] Comorbidities included heart disease, stroke, hypertension, airway disease (asthma, chronic bronchitis or chronic obstructive pulmonary disease (COPD)), diabetes, stomach disease, kidney disease, liver disease, anemia or other blood disease, thyroid disease, depression, arthrosis, back pain, and rheumatic disease.

The Brief Illness Perception Questionnaire (B-IPQ) was used to assess IPs.[21] The B-IPQ includes eight items. Test-retest reliability (Pearson correlations 0.42-0.75) of the items is fair.[21] Similar to earlier studies[22-25], a 2-factor structure was found using principal components factor analysis. A multi-item scale was computed of 5 BIPQ items selected through the factor analysis (factor loadings > 0.70), and included consequences ("How much does your illness affect your life?"), timeline ("How long do you think your illness will continue?"), identity ("How much do you experience symptoms from your illness?"), concern ("How concerned are you about your illness?"), and emotional response ("How much does your illness affect you emotionally?"). A multi-item scale was computed of these items by averaging the item scores, when ≤1 item response was missing. The internal consistency of the scale was good (standardized Cronbach alpha,.85). Higher scores indicated more threatening IPs.

Prognosis at the time of the questionnaire was determined by conditional 5-year relative survival (ie, the probability of surviving an additional 5 years on the condition that the patient has survived x number of years after diagnosis). Estimates were calculated using data from the NCR, including mortality data from patients diagnosed between 1989 and 2008 who were followed for up to 15 years, and were determined by years survived after diagnosis, tumor type, tumor stage, age group (ages 15-44 years, ages 45-59 years, ages 60-74 years, and ages 75-89 years), and sex. Conditional relative survival data from the NCR has been described previously for colorectal[26] and prostate[27] cancer, and Non-Hodgkin Lymphoma[28]. For endometrial and ovarian cancer survivors in our sample, who were included within one year after diagnosis, 5-year survival at time of diagnosis by cancer stage was determined (www.cijfersoverkanker.nl).

To create the optimistic, realistic, and pessimistic IP groups, the sample was divided into conditional 5-year relative survival strata (<60%, 60%-69%, 70%-79%, 80%-89%, and 90%-100%). Then, in each stratum, quartiles of BIPQ multi-item scores were defined. Survivors with the lowest quartile of BIPQ scores in their stratum (<25%) were allocated to "pessimistic" IP, those with interquartile scores (25%-75%) were allocated to "realistic" IP, and those with the highest quartile (>75%) were allocated to "optimistic" IP (Table 1).
The European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30; version 3.0) was used to assess HRQoL among the participants.[29] The scores were linearly transformed into a score between 0 and 100.[30] Higher scores on the functioning scales indicated better functioning and global QOL, whereas higher scores on the symptom scales indicated more symptom complaints and financial difficulties. Vital status and date of death data were obtained from the Dutch municipal personal records database and last were verified on February 1, 2017. Anxiety and depression were measured in survivors of colon cancer, rectal cancer, and lymphoma using the Hospital Anxiety and Depression Scale (HADS)[31] The HADS assesses separate anxiety and depression scales, both of which consist of 7 items. Higher scores indicate more anxiety and depressive symptoms.

Statistical analysis

Statistical analyses were conducted using SAS statistical software (version 9.4; SAS Institute Inc, Cary, North Carolina). Frequencies with percentages and means with standard deviations were used to describe the baseline characteristics, and chi-square tests, independent Student *t* tests, and Mann-Whitney *U* tests were used to test the differences between patients with optimistic, realistic, and pessimistic IPs. *P* values < .05 were considered to be statistically significant.

Correlations were computed to assess whether BIPQ items were interrelated with HRQoL scales. General linear models were conducted to assess differences in HRQoL between survivors with optimistic, realistic, and pessimistic IPs. Bonferroni-corrected pairwise comparisons were made to compare survivors with optimistic versus realistic IPs and pessimistic versus realistic IPs, adjusted for a priori selected covariates (age at the time of the questionnaire, sex, educational level, years from diagnosis, tumor type, tumor stage, treatment [surgery, radiotherapy, or systemic therapy], number of comorbidities, employment, and marital status). Additional analyses were adjusted for anxiety and depression.

Kaplan-Meier curves were conducted to show differences in survival between the 3 subgroups. A Cox proportional hazards regression model was performed to assess differences in survival between patients with optimistic, realistic, and pessimistic IPs. The survival duration was specified as the time from the questionnaire until either death or

the censoring date (February 1, 2017). To adjust for survivorship bias, a variable with the left truncation time (time between diagnosis and questionnaire) was added as an argument and the time of the questionnaire was set as the entry time. In addition, the model was adjusted for covariates controlling for factors influencing survival (age at the time of the questionnaire, sex, educational level, tumor type, tumor stage, treatment [surgery, radiotherapy, or systemic therapy], number of comorbidities, employment, and marital status).

RESULTS

A total of 3882 cancer survivors were invited to participate in 1 of the 5 studies, 2744 of whom (71%) returned the questionnaire. The current analysis included 2457 cancer survivors (63%) for whom no data were missing regarding the grouping variable (tumor stage to determine prognosis, BIPQ scale) (see Supporting Fig. 1). Cancer survivors were classified into those with optimistic (582 survivors), realistic (1230 survivors), and pessimistic (645 survivors) IPs (Table 1).

Compared with survivors with realistic IPs, those with optimistic IPs tended to be older, were more often male, were more often survivors of colon cancer and less often survivors of rectal and ovarian cancer, had lower stages of disease, had fewer comorbidities, and were less often employed. Survivors with pessimistic IPs tended to be younger, were more often female, were more often less educated, were less often survivors of colon cancer and more often survivors of rectal cancer, had more comorbidities, less often had a partner, and more often received radiotherapy (Table 2).

Table 1: Group allocation of survivors into 'optimistic', 'realistic' and 'pessimistic' IPs within 5-year conditional survival strata

		Quartiles of illness perception scores[b]		
Prognosis at time of questionnaire (Conditional 5-year relative survival[a])	N Total=2,457	<25th 'optimistic' (N=582)	25th-75th 'Realistic' (N=1,230)	>75th 'Pessimistic' (N=645)
<60%	148	<4.4	4.4-7.3	>7.3
60-69%	234	<2.4	2.4-6.2	>6.2
70-79%	384	<2.4	2.4-5.8	>5.8
80-89%	806	<2.6	2.6-6.0	>6.0
90-100%	885	<2.0	2.0-5.2	>5.2

Abbreviation: IPs, illness perceptions. [a]The IPs score was based on the average of Brief Illness Perception Questionnaire (BIPQ) scores (1-10) of items selected in factor analysis (consequences, timeline, identity, concern, and emotional response). A higher score indicates more threatening IPs. [b]The probability of surviving an additional 5 years on the condition that the patient has survived x number of years after diagnosis, based on years survived from diagnosis, tumor type, tumor stage, age group, and sex.

Table 2: Sociodemographic and clinical characteristics of survivors with optimistic, realistic or pessimistic IPs

	Total (N=2,457)	Optimistic IPs (N=582)	Realistic IPs (N=1,230)	Pessimistic IPs (N=645)	Optimistic versus Realistic, P-value	Pessimistic versus Realistic, P-value
Age at survey						
Mean (SD)	68.1 (10.1)	69.3 (9.5)	68.3 (10.3)	66.7 (10.2)	**0.03**	**<0.01**
Sex, n(%)						
Male	1,457 (59)	380 (65)	730 (59)	347 (54)	**0.02**	**0.02**
Female	1,000(41)	202 (35)	500 (41)	298 (46)		
Education, n (%)						
Lower education						
Secondary education (high school)						
Secondary (vocational) education	420 (17)	91 (22)	200 (48)	129 (20)		
Higher (vocational) education, university	684 (28)	153 (22)	341 (28)	190 (30)		
	823 (34)	195 (34)	412 (34)	216 (34)		
	504 (21)	139 (28)	260 (52)	105 (16)	0.63	**0.03**
Years from diagnosis						
Median (IQR)	2.7 (1.9-3.6)	2.8 (2.0-3.7)	2.7 (1.9-3.6)	2.6 (1.9-3.6)		
<2	680 (17)	150 (26)	345 (28)	185 (29)		
2-3	809 (21)	190 (33)	411 (33)	208 (32)	0.40	0.60
3-4	968 (25)	242 (42)	474 (39)	252 (26)	0.42	0.86
Cancer type, n (%)						
Colon						
Rectal		239 (41)	356 (46)	184 (24)		
Prostate	779 (32)	79 (14)	227 (18)	143 (22)		
Ovarian	449 (18)	107 (18)	297 (24)	112 (17)		
Endometrial	516 (21)	16 (3)	79 (6)	47 (7)		
Non-Hodgkin	142 (6)	42 (7)	112 (9)	43 (7)		
Lymphoma (aggressive)	197 (8)	78 (13)	87 (7)	63 (28)		
Non-Hodgkin	228 (9)					
Lymphoma (indolent)	146 (6)	21 (4)	72 (6)	53 (8)	**<0.01**	**<0.01**
Comorbidity, n (%)						
None	742 (30)	215 (37)	381 (31)	146 (23)		
1	714 (29)	182 (31)	361 (29)	171 (27)		
2 or more	1001 (41)	185 (18)	488 (40)	328 (51)	**<0.01**	**<0.01**
Marital status, n (%)						
Partner	1,949 (80)	456 (79)	992 (81)	501 (78)		
No partner	484 (20)	119 (21)	226 (19)	139 (29)	0.28	0.10
Employed, n (%)						
Yes	444 (19)	94 (17)	238 (120)	112 (18)		
No	1,939 (81)	473 (83)	952 (80)	514 (82)	0.09	0.28
TNM/ Ann Arbor stage, n (%)						
I	627 (25)	154 (25)	317 (26)	156 (24)		
II	931 (38)	243 (42)	449 (37)	239 (37)		
III	683 (28)	157 (27)	355 (29)	171 (27)		
IV	195 (8)	23 (4)	99 (8)	73 (37)	**0.01**	0.18
Treatment, n (%)						
Surgery	1,696 (69)	412 (71)	845 (69)	439 (68)	0.37	0.78
Radiotherapy	688 (28)	138 (20)	338 (27)	212 (31)	0.0	**0.01**
Systemic therapy	818 (33)	183 (31)	406 (33)	229 (36)	0.51	0.28

Abbreviations: IPs, illness perceptions; IQR, interquartile range; SD, standard deviation. Percentages do not always add up to 100 because they were rounded off to whole numbers. [a]Bold type indicates statistical significance.

Table 3: General linear models comparing HRQoL and symptoms between cancer survivors with optimistic, realistic and pessimistic IP. Crude means (M) and standard deviations (SD) are shown.

	Total (N=2,457)	Optimistic IPs (N=582)	Realistic IPs (N=1,230)	Pessimistic IPs (N=645)	Optimistic versus Realistic, p-value[a] (size of difference)	Pessimistic versus Realistic, p- value[a] (size of difference)
Global quality of life	75.0 (19)	85.2 (14)	77.1 (16)	61.9 (22)	<0.01 (S)	<0.01 (L)
Functioning scales						
Physical functioning	80.5 (20)	88.0 (15)	82.4(18)	70.1 (23)	<0.01 (S)	<0.01 (S)
Social functioning	85.0 (23)	95.5 (12)	88.0 (19)	70.0 (29)	<0.01 (S)	<0.01 (L)
Cognitive functioning	83.7 (21)	90.2 (15)	85.1 (19)	75.2 (26)	<0.01 (S)	<0.01 (M)
Emotional functioning	84.4 (20)	94.4 (11)	87.4 (17)	69.9 (24)	<0.01	<0.01
Role functioning	77.8 (28)	89.8 (19)	80.2 (25)	62.4 (33)	<0.01 (S)	<0.01 (S)
Symptom scales						
Fatigue	25.1 (25)	13.4(17)	23.0 (22)	40.0 (27)	<0.01 (S)	<0.01 (M)
Nausea/ vomiting,	4.4 (13)	1.7 (7)	3.4 (11)	8.5 (18)	<0.01 (T)	<0.01 (S)
Pain	17.5(25)	9.5 (18)	15.7 (23)	28.3 (30)	<0.01 (S)	<0.01 (S)
Dyspnoea	15.3 (25)	8.2 (19)	13.4 (23)	25.4 (31)	<0.01 (S)	<0.01 (M)
Insomnia	21.8 (30)	11.7 (22)	20.3 (28)	33.6 (34)	<0.01 (S)	<0.01 (M)
Appetite loss	6.8 (18)	2.7 (11)	5.3 (16)	13.5 (25)	<0.01 (T)	<0.01 (S)
Constipation	9.4 (21)	5.2 (15)	9.3 (20)	13.3 (25)	<0.01 (T)	<0.01 (T)
Diarrhoea	9.6 (21)	5.0 (14)	9.2 (20)	14.1 (26)	<0.01 (S)	<0.01 (S)
Financial problems	7.2 (19)	2.7 (11)	5.4 (16)	14.7 (26)	<0.01 (T)	<0.01 (S)

Abbreviations: HRQOL, health-related quality of life; IP, illness perception; L, large difference, M, medium difference; S, small difference; SD, standard deviation; T, trivial difference. [a]Analyses were adjusted for age at the time of the survey, sex, educational level, years from diagnosis, tumor type, tumor stage, treatment (surgery, radiotherapy, or systemic therapy), number of comorbidities, employment, and marital status. Higher scores on global QOL and functioning scales and lower scores on symptom scales indicate a better HRQOL. The size of the mean difference was determined based on guidelines of clinical relevance from Cocks et al.[32] The guideline for the emotional functioning subscale is unknown.

Correlations between BIPQ items that were included in the IPs scale were weak to moderate (correlation coefficient, -0.53 to 0.45) (see Appendix 1). For all HRQOL scales, functioning and global QOL were higher and symptom burden was lower in those with optimistic IPs compared with those with realistic IPs (all $P < .01$). According to guidelines for clinical relevance, mean differences were trivial or small.[32] Functioning was lower and symptoms were higher in those with pessimistic IPs compared with those with realistic IPs (all $P < .01$), and mean differences were trivial to large (Table 3).[32] Differences remained significant after additional adjustment for anxiety and depression, and when analyses were stratified by prognosis group.

Overall, all-cause mortality was found to be higher in survivors with pessimistic IPs compared with those with realistic IPs (adjusted hazard ratio, 1.52; 95% confidence interval, 1.27-1.84 [$P < .01$]). In addition, all-cause mortality was found to be slightly but significantly lower in survivors with optimistic IPs compared with those with realistic IPs (adjusted hazard ratio, 0.72; 95% confidence interval, 0.57-0.90 [$P < .05$]) (Table 4) (Fig. 1).

Table 4: Cox hazard regression models for optimistic versus realistic and pessimistic versus realistic IP

	N	Person-Years	Deaths	Unadjusted HR (95% CI)	Adjusted HR[a] (95% CI)
Total					
Realistic IPs	582	6194.4	288	1.00 (ref)	1.00 (ref)
Optimistic IPs	1,230	3159.4	106	**0.74 (0.58-0.91)****	**0.72 (0.57-0.90)****
Pessimistic IPs	645	3065.2	218	**1.52 (1.28-1.81)****	**1.52 (1.27-1.84)****

Abbreviations: 95% CI, 95% confidence interval; HR, hazard ratio; IPs, illness perceptions. a Bold type indicates statistical significance. b Adjusted for age at the time of the survey, sex, educational level, tumor type, tumor stage, treatment surgery, radiotherapy, or systemic therapy), number of comorbidities, employment, and marital status. c $P < .01$. d $P < .05$.

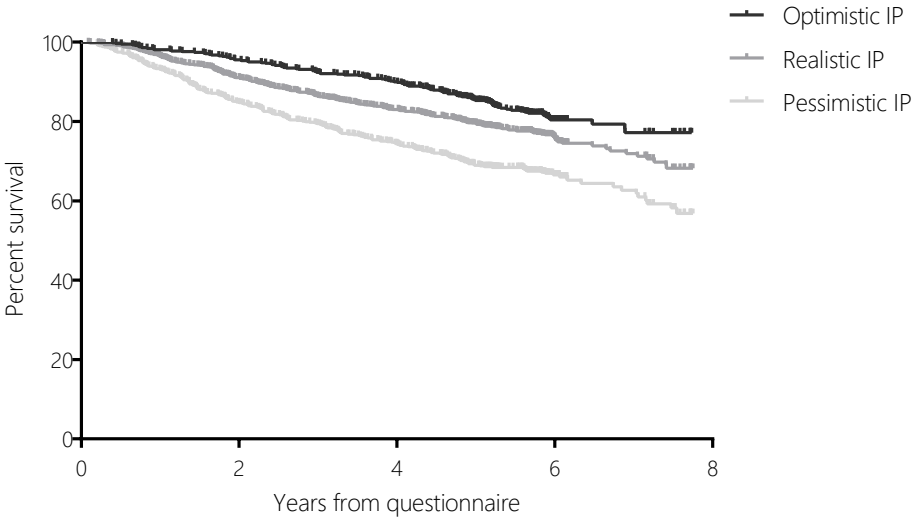


Figure 1: Kaplan-Meier survival curves of survivors with optimistic, realistic and pessimistic IPs

DISCUSSION

We demonstrated that having optimistic IPs, even when they may appear unrealistic with respect to prognosis, are associated with higher HRQoL and lower mortality, whereas having pessimistic IPs are associated with poorer outcomes compared with IPs that are consistent with disease severity (ie, realistic IPs). This violates our hypothesis that realistic IPs are more beneficial than more optimistic IPs, and demonstrates that IPs are important predictors of survivors' health outcomes regardless of disease prognosis. In addition, the comparison of the 3 IPs groups in the current study elucidated that differences in outcomes were much larger between the pessimistic IPs group and the realistic IPs group compared with between the optimistic and realistic IPs groups, specifically with respect to social functioning, cognitive functioning, fatigue, nausea, insomnia, and global QoL.

Similar to previous work focusing on the relationship between IPs and physical and psychological outcomes, including HRQoL, psychological distress, and mortality,[2-10] we found that less threatening (ie, more positive) IPs were associated with more favorable outcomes, whereas more threatening (ie, more negative) IPs were associated with unfavorable outcomes. The results of the current study demonstrate that IPs are associated with HRQoL and survival independent of disease severity (ie, prognosis). According to the common sense model of self-regulation of Leventhal et al, the relationship between IPs and health outcomes is mediated through coping.[33] Accordingly, threatening IPs have been associated with passive coping strategies, such as anxious preoccupation and helplessness/hopelessness among cancer survivors,[4]which may explain the relation to poor health outcomes. An alternative explanation may be that the IPs in the current study simply were a more inclusive reflection of disease severity, comprising symptoms, disease progression, and comorbidities. This is in parallel with self-rated health as an inclusive measure of health status, reflecting bodily sensations or symptoms indicating physiological dysregulations or preclinical disease,[34,35] as well as internal or external resources that affect health (ie, educational level, financial status and social support, optimism, or self-control).[36] Inclusiveness also may explain why IPs in the current study appeared to be predictive of health outcomes independent of prognosis, reflecting that all groups in the current study were rather "realistic" about their outcomes.

Consistent with literature regarding threatening IPs, pessimistic IPs were found to be associated with sociodemographic factors, including younger age, being female, and having a low educational level.[37,38]. In addition, we found that higher cancer stage and more comorbidities were associated with having pessimistic IPs. Furthermore, survivors with pessimistic IPs more often received radiotherapy, which previously has been associated with higher levels of psychological distress,[39], fatigue [40] and a lower HRQoL.

Limitations

Using comprehensive historical cancer registry data to estimate prognosis at the time of the questionnaire, we tried to adjust for the (clinical) factors that interfere with IPs and health outcomes (ie, years from diagnosis, cancer stage at the time of diagnosis, patient age and sex). However, other factors comprising prognosis were not covered in this estimate, such as comorbidities, disease progression, or disease recurrence. For example, the high prevalence of comorbidities in the group with pessimistic IPs may explain their low survival. Although adjustment for comorbidities at the time of the questionnaire did not alter the current study results, we could not adjust for comorbidities at the time of diagnosis or in the years after questionnaire completion. In addition, no data were available regarding disease progression or recurrence. The inclusion of survivors with recurrent disease may have inflated the results of the current study because these individuals were likely allocated to the pessimistic IPs group and inevitably had poorer health outcomes.

Furthermore, our composite BIPQ scale was based on a factor structure that was similar to that of other studies,[22-25], but does not support the theoretical model by Leventhal etal that presents emotional and cognitive representations as distinct factors. As a consequence, the groups in the current study were not only based on cognitive perceptions regarding disease severity, such as perceptions of how long the disease will continue, but also on emotional representations. Therefore, it is not surprising that the groups were strongly associated with HRQoL subscales. To further elucidate whether more optimistic perceptions of prognosis are indeed more beneficial for cancer survivors than (clinically) accurate perceptions of prognosis, a prognostic awareness measure could be used to create the groups, similar to the questionnaires used in palliative research.[41] In addition, use of supportive care services should be measured as this may influence survivors' IPs.

The current study included a large and heterogeneous sample of survivors of various cancer types, but there were relatively many survivors with favorable prognoses, and a lack of common cancer types such as breast and lung cancer. Thus, despite our high response rate (71%), the findings of the current study may not be fully generalizable to other cancer survivor populations. Furthermore, although our survival analyses demonstrated longitudinal associations, we could not confirm the causal relationship between IPs and HRQoL using a cross-sectional survey. Longitudinal surveys are needed to confirm the long-term benefit of optimistic perceptions of illness and prognosis. It also should be noted that our groups were created based on quartile cutoff values of the BIPQ scores, which are clinically arbitrary and are not validated using specific questionnaires for optimistic, realistic, or pessimistic IPs. Future studies are needed to confirm these IP groups in other cancer survivor populations.

Future directions

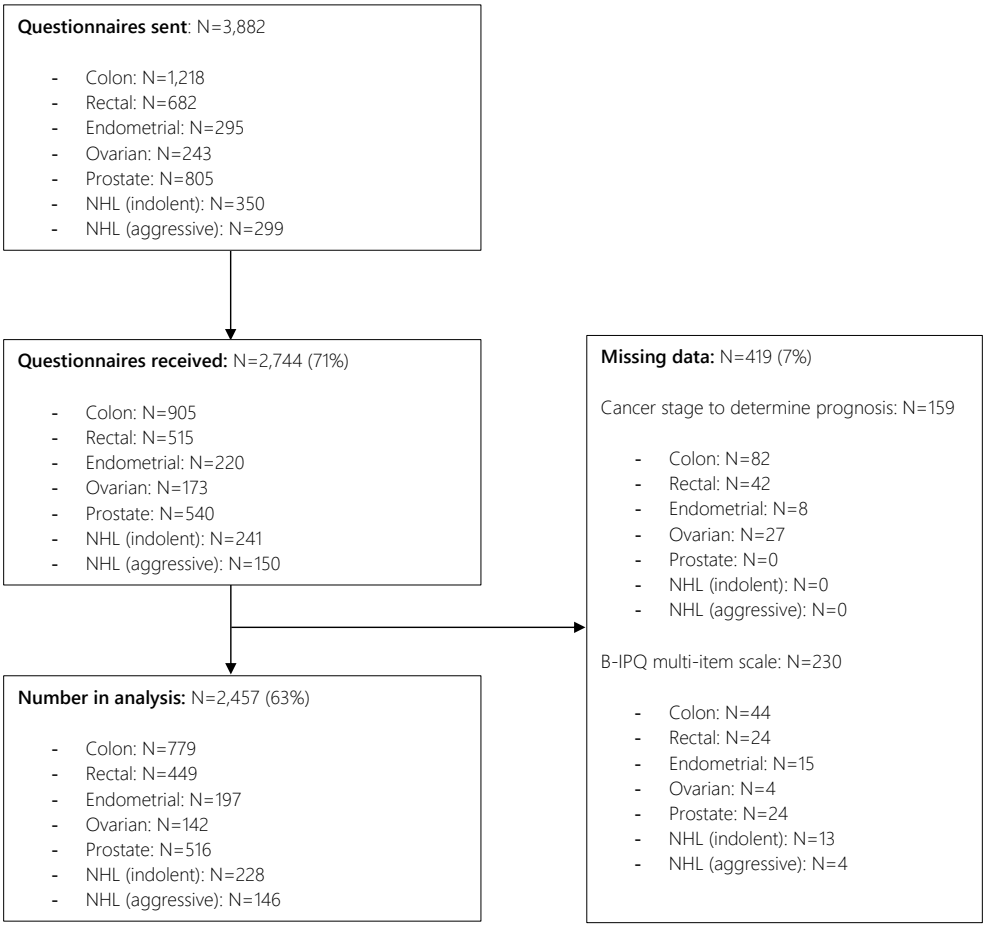
Although we acknowledge that the current study had limitations with regard to its design and the availability of data, and that further research is needed, we believe that its results provide valuable new insights into the importance of IPs among cancer survivors in relation to HRQoL and survival. The classification of survivors into groups based on IPs relative to their prognosis is a novel way with which to assess the impact of having threatening IPs on health outcomes, in contrast to a body of literature focusing on linear relationships between IPs and outcomes.[2-10] In a previous trial in which survivorship care plans were found to provide accurate and honest diagnostic and prognostic information, they induced more threatening IPs among cancer survivors.[11-13] Because the results of the current study indicate that holding realistic or pessimistic IPs may be associated with lower HRQoL and survival, we may need to be careful when providing information to survivors, such as diagnostic or prognostic information. However, further research regarding this topic is warranted. Therefore, future interventions that include diagnostic or prognostic

information should include an assessment of the potential harmful effects through more threatening IPs. Furthermore, rather than assuming that we need to encourage survivors with pessimistic IPs to be more optimistic, we believe it is important to understand why these individuals have pessimistic or threatening IPs. It is possible that their perceptions are a much more inclusive reflection of their state of health than a set of objective measures comprises.[36]

Survivors with IPs that are relatively optimistic with respect to their prognosis appear to have the most favorable health outcomes, whereas those with pessimistic IPs relative to their prognosis have the worst outcomes compared with those with realistic IPs. Hence, IPs may be important predictors of health outcomes independent of prognosis. We need to acknowledge the pessimistic or threatening IPs among cancer survivors and provide support that is appropriate for this group to improve their outcomes.

APPENDIX I

Flow chart of survivors included in analysis



REFERENCES

1. Hagger MS, Orbell S. A meta-analytic review of the common-sense model of illness representations. *Psychology and health.* 2003;18(2):141-184.
2. Ashley L, Marti J, Jones H, Velikova G, Wright P. Illness perceptions within 6 months of cancer diagnosis are an independent prospective predictor of health-related quality of life 15 months post-diagnosis. *Psycho-oncology.* Nov 2015;24(11):1463-1470.
3. Gray NM, Hall SJ, Browne S, et al. Modifiable and fixed factors predicting quality of life in people with colorectal cancer. *British journal of cancer.* May 24 2011;104(11):1697-1703.
4. Hopman P, Rijken M. Illness perceptions of cancer patients: relationships with illness characteristics and coping. *Psycho-oncology.* Jan 2015;24(1):11-18.
5. Keeling M, Bambrough J, Simpson J. Depression, anxiety and positive affect in people diagnosed with low-grade tumours: the role of illness perceptions. *Psycho-oncology.* Jun 2013;22(6):1421-1427.
6. Millar K, Purushotham AD, McLatchie E, George WD, Murray GD. A 1-year prospective study of individual variation in distress, and illness perceptions, after treatment for breast cancer. *Journal of psychosomatic research.* Apr 2005;58(4):335-342.
7. Rozema H, Vollink T, Lechner L. The role of illness representations in coping and health of patients treated for breast cancer. *Psycho-oncology.* Aug 2009;18(8):849-857.
8. Scharloo M, Baatenburg de Jong RJ, Langeveld TP, van Velzen-Verkaik E, Doorn-op den Akker MM, Kaptein AA. Quality of life and illness perceptions in patients with recently diagnosed head and neck cancer. *Head & neck.* Oct 2005;27(10):857-863.
9. Thong MS, Kaptein AA, Vissers PA, Vreugdenhil G, van de Poll-Franse LV. Illness perceptions are associated with mortality among 1552 colorectal cancer survivors: a study from the population-based PROFILES registry. *Journal of cancer survivorship : research and practice.* Oct 2016;10(5):898-905.
10. Traeger L, Penedo FJ, Gonzalez JS, et al. Illness perceptions and emotional well-being in men treated for localized prostate cancer. *Journal of psychosomatic research.* Nov 2009;67(5):389-397.
11. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Survivorship care plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients: the ROGY care trial. *Quality of Life Research.* 2018:1-12.
12. de Rooij BH, Ezendam NPM, Nicolaije KAH, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecologic oncology.* May 2017;145(2):319-328.
13. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
14. Clayton JM, Hancock K, Parker S, et al. Sustaining hope when communicating with terminally ill patients and their families: a systematic review. *Psycho-oncology.* Jul 2008;17(7):641-659.
15. Hancock K, Clayton JM, Parker SM, et al. Truth-telling in discussing prognosis in advanced life-limiting illnesses: a systematic review. *Palliative medicine.* 2007;21(6):507-517.
16. Walshe C, Roberts D, Appleton L, et al. Coping well with advanced cancer: a serial qualitative interview study with patients and family carers. *PloS one.* 2017;12(1):e0169071.
17. van de Poll-Franse LV, Horevoorts N, van Eenbergen M, et al. The Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship registry: scope, rationale and design of an infrastructure for the study of physical and psychosocial outcomes in cancer survivorship cohorts. *European Journal of Cancer.* 2011;47(14):2188-2194.
18. Fritz A, Percy C, Jack A, et al. *International classification of diseases for oncology.* World Health Organization; 2000.
19. Sobin LH, Gospodarowicz MK, Wittekind C. *TNM classification of malignant tumours*. John Wiley & Sons; 2011.
20. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis Care & Research.* 2003;49(2):156-163.

21. Broadbent E, Petrie KJ, Main J, Weinman J. The brief illness perception questionnaire. *Journal of psychosomatic research.* Jun 2006;60(6):631-637.
22. Karatas T, Ozen S, Kutluturkan S. Factor Structure and Psychometric Properties of the Brief Illness Perception Questionnaire in Turkish Cancer Patients. *Asia Pac J Oncol Nurs.* Jan-Mar 2017;4(1):77-83.
23. Schuz B, Wolff JK, Warner LM, Ziegelmann JP, Wurm S. Multiple illness perceptions in older adults: effects on physical functioning and medication adherence. *Psychology & health.* 2014;29(4):442-457.
24. Timmermans I, Versteeg H, Meine M, Pedersen SS, Denollet J. Illness perceptions in patients with heart failure and an implantable cardioverter defibrillator: Dimensional structure, validity, and correlates of the brief illness perception questionnaire in Dutch, French and German patients. *Journal of psychosomatic research.* Jun 2017;97:1-8.
25. Zhang N, Fielding R, Soong I, et al. Psychometric assessment of the Chinese version of the brief illness perception questionnaire in breast cancer survivors. *PloS one.* 2017;12(3):e0174093.
26. Van Erning F, Van Steenbergen L, Lemmens V, et al. Conditional survival for long-term colorectal cancer survivors in the Netherlands: who do best? *European Journal of Cancer.* 2014;50(10):1731-1739.
27. Husson O, Steenbergen LN, Koldewijn EL, Poortmans PM, Coebergh JWW, Janssen-Heijnen ML. Patients with prostate cancer continue to have excess mortality up to 15 years after diagnosis. *BJU international.* 2014;114(5):691-697.
28. van de Schans SA, van Steenbergen LN, Coebergh JWW, Janssen-Heijnen ML, van Spronsen DJ. Actual prognosis during follow-up of survivors of B-cell non-Hodgkin lymphoma in the Netherlands. *Haematologica.* 2014;99(2):339-345.
29. Niezgoda HE, Pater J. A validation study of the domains of the core EORTC quality of life questionnaire. *Quality of Life Research.* 1993;2(5):319-325.
30. Fayers P, Aarson N, Bjordal K, Sullivan M. QLQ C-30 scoring manual/EORTC Study Group on Quality of Life. Brussels; 1995.
31. Spinhoven P, Ormel J, Sloekers P, Kempen G, Speckens A, Van Hemert A. A validation study of the Hospital Anxiety and Depression Scale (HADS) in different groups of Dutch subjects. *Psychological medicine.* 1997;27(02):363-370.
32. Cocks K, King MT, Velikova G, Martyn St-James M, Fayers PM, Brown JM. Evidence-based guidelines for determination of sample size and interpretation of the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jan 01 2011;29(1):89-96.
33. Leventhal H, Meyer D, Nerenz D. The common sense representation of illness danger. *Contributions to medical psychology.* 1980;2:7-30.
34. Halford C, Anderzen I, Arnetz B. Endocrine measures of stress and self-rated health: a longitudinal study. *Journal of psychosomatic research.* Oct 2003;55(4):317-320.
35. Idler EL, Benyamini Y. Self-rated health and mortality: a review of twenty-seven community studies. *Journal of health and social behavior.* Mar 1997;38(1):21-37.
36. Benyamini Y. Why does self-rated health predict mortality? An update on current knowledge and a research agenda for psychologists. *Psychology & health.* Nov 2011;26(11):1407-1413.
37. Zhang N, Fielding R, Soong I, et al. Illness perceptions among cancer survivors. *Supportive Care in Cancer.* 2016;24(3):1295-1304.
38. Aalto A-M, Heijmans M, Weinman J, Aro AR. Illness perceptions in coronary heart disease. *Journal of psychosomatic research.* 2005;58(5):393-402.
39. Hervouet S, Savard J, Simard S, et al. Psychological functioning associated with prostate cancer: cross-sectional comparison of patients treated with radiotherapy, brachytherapy, or surgery. *Journal of pain and symptom management.* 2005;30(5):474-484.
40. Ahlberg K, Ekman T, Gaston-Johansson F. The experience of fatigue, other symptoms and global quality of life during radiotherapy for uterine cancer. *International journal of nursing studies.* 2005;42(4):377-386.
41. El-Jawahri A, Traeger L, Park ER, et al. Associations among prognostic understanding, quality of life, and mood in patients with advanced cancer. *Cancer.* 2014;120(2):278-285.

Part III: information and care needs

7

Chapter 7

Cluster analysis demonstrates the need to individualize care for cancer survivors

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ABSTRACT

Background: In efforts to inform clinical screening and development of survivorship care services, we sought to characterize patterns of healthcare needs among cancer survivors by 1) identifying and characterizing subgroups based on self reported health care needs, and 2) assessing socio-demographic, clinical and psychosocial factors associated with these subgroups.

Methods: We conducted a cross-sectional self administered survey among patients presenting for routine follow-up care for early stage cancer at our academic medical center. Latent class cluster analysis was used to identify clusters of survivors based on survivorship care needs within 7 domains. Multiple logistic regression analyses were used to assess factors associated with these clusters.

Results: Among 292 respondents, the highest unmet needs were related to information regarding side effects (53%), self-care (51%) and emotional coping (43%) domains. Our analysis identified 4 clusters of survivors: 1) low needs (N=123, 42%), 2) mainly physical needs (N=46, 16%), 3) mainly psychological needs (N=57, 20%) and 4) both physical and psychological needs (N=66, 23%). Compared to cluster 1, those in clusters 2, 3, and 4 were younger ($P<0.03$); those in clusters 3 and 4 had higher levels of psychological distress ($P<0.05$); and those in clusters 2 and 4 reported higher levels of fatigue ($P<0.05$).

Conclusions: Unmet needs among cancer survivors are prevalent, however a substantial group of survivors report low or no healthcare needs. The wide variation in healthcare needs among cancer survivors suggests a need for screening all patients, followed by tailored interventions in clinical care delivery and research.

INTRODUCTION

Due to advances in health care and ageing of the population, the number of cancer survivors is increasing. In the United States, there were approximately 15.5 million cancer survivors in 2016, and this number is expected to exceed 20.3 million by 2026.[1] This growing group of cancer survivors often faces physical and psychosocial issues as a result of cancer and cancer treatment[2]. Previous work has found that survivors have unmet needs regarding management of persistent complications from cancer therapy, practical assistance in daily living, and help with psychosocial problems such as anxiety and fear of recurrence.[3-5] However, the level and type of needs differ across survivor populations and settings.[6] Identifying needs clusters, as opposed to focusing only on distinct individual symptoms and problems, may provide insight into the challenges faced by cancer survivors and the best way to address them.

Over the past decades, the need to identify and address health concerns for patients who are expected to live years beyond initial therapy for cancer (defined as cancer survivors, for purposes of this paper) has been well described.[7,8] In the American Institute of Medicine's (IOM) report, "*From cancer patient to cancer survivor, lost in transition*," Survivorship Care Plans (SCPs) containing a treatment summary and follow-up care plan were advocated as an available and efficient means to meet the needs of cancer survivors[7]. Although the face validity of SCPs seemed acceptable, several randomized controlled trials have failed to identify beneficial effects of SCPs in various study populations.[9-12] In addition, the provision of SCPs has shown to be more resource intensive than anticipated, resulting in low implementation and dissemination of SCPs in clinical practice.[13-15] However, SCPs may be beneficial for subgroups of patients, particularly underserved populations.[16] Consequently, debates on how best to address the needs of cancer survivors persist.[6,17,18]

The optimal method to effectively and efficiently identify and address needs of cancer survivors remains undefined. Because cancer survivors constitute a heterogeneous population with different cancer types, treatment plans, ongoing/maintenance therapy, long term health risks, individual health care needs and preferences, we sought to determine if distinct subgroups of patients could be identified with similar needs that might be addressed through select group interventions and services. In this study, we present a cluster analysis based on individual self-reported care needs among cancer survivors that aims to 1) characterize subgroups of patients with similar patterns of health care needs and 2) assess the socio-demographic, clinical and psychosocial factors associated with these subgroups.

METHODS

Study design

We conducted a cross-sectional self-administered comprehensive needs assessment survey. All English speaking adult patients with a history of cancer presenting for follow-up care to the Massachusetts General Hospital Cancer Center between February and July of 2016 were eligible to participate. Only English questionnaires were used due to our pragmatic method of survey distribution. Surveys were provided by clinicians in clinic, research assistants in the waiting rooms, and clinic staff at the check-in desk across multiple disease specific clinics and two affiliated community oncology practices. Due to the pragmatic method of survey distribution, the number of patients offered or eligible for the survey cannot be assessed. The Dana-Farber/Harvard Cancer Center institutional review board approved the study.

Study population

A total of 636 patients participated in the survey. For the purposes of this analysis, we included only patients participating in the cancer center wide survey who self-identified as having no evidence of distant metastases and who were a) on therapy with curative intent within 2 years of cancer diagnosis, b) on adjuvant endocrine therapy or c) off therapy in long term follow-up. Patients reporting incurable cancer, or reporting curable cancer but currently receiving radiation therapy or chemotherapy greater than 2 years from the time of diagnosis (indicating potential stage IV disease) were excluded (N=298). In addition, patients with early stage disease that did not complete the survivorship care needs assessment (N=46) were excluded from the current analysis.

Measures

Socio-demographic variables included age, gender, race, marital status, employment, internet access, educational level and income. Clinical variables included cancer type category, years since diagnosis, treatment (both current and previous), and number of listed comorbidities.

Survivorship care needs

The comprehensive needs assessment survey was developed by a multidisciplinary team of health services researchers, oncologists, psychologists, nurses, and primary care physicians with input from patients and family members of patients. The survey included 66 study-specific items on information to help survivors cope with their cancer or treatments, subdivided into seven domains: side-effects, lifestyle/self-care, emotional coping, social support, sexual health, complementary services and practical support. Participants were asked to report the concern ('I do have this problem') and to indicate their interest in receiving information to help them cope with this concern ('I have enough

information', 'Not at all interested', 'A little interested' and 'Very interested'). All items were dichotomized into needs ('A little interested/ 'very interested) versus no needs (no concern indicated, 'I have enough information', or 'not at all interested'). For each of the seven domains, a dichotomous scale was computed based on needs in domain (needs on at least one item in domain) versus no needs in domain. Internal consistency of the domain scales in our sample was good (Cronbach's Alpha's, side effects= 0.89; emotional coping=0.88; social support=0.88; lifestyle/self care=0.77; sexual health=0.75; complementary services=0.91; practical support=0.74).

Emotional and physical symptoms

Fear of recurrence was measured using the revised 5-item Assessment of Survivor Concerns (ASC).[19] Internal consistency of the scale in our sample was good (Cronbach's Alpha = 0.88). Depression, anxiety, insomnia, pain and fatigue were single-item scales based on a modified version of the FACT-G.[20] Items were measured on a 5-point Likert frequency scale ('never', 'rarely', 'sometimes', 'very often' and 'always'), and included depression ('I feel sad or depressed'), anxiety ('I feel nervous or worried'), insomnia ('I have problems falling or staying asleep'), pain ('I have pain') and fatigue ('my fatigue interferes with my usual activities'). Higher scores indicate greater problems.

Statistical Analysis

Latent class cluster analysis was conducted to identify clusters of cancer survivors based on survivorship care needs across seven domains. Latent class modeling is a data-driven approach, which aims to classify similar objects, with respect to a set of variables, into mutually exclusive groups.[21] Variables used to define the need-clusters were seven dichotomous scales indicating needs in domain. The optimal number of clusters was derived from goodness-of-fit statistics. Bivariate residuals were assessed to check if the local independency assumption was met (values <3).[21] Cluster analyses were conducted with Latent GOLD version 5.2.0 (Statistical Innovations Inc., Belmont, MA, USA).

Further statistical analyses were conducted using Statistical Analysis System (SAS) version 9.4. (SAS Institute, Cary, NC, 1999). Differences in baseline characteristics between need-clusters were assessed using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables. Characteristics that differed across clusters ($P \leq 0.1$) were entered into a multiple logistic regression analysis. Both univariate and multivariate models were built to assess the odds that a cancer survivor was in a need-cluster as indicated by the conditional socio-demographic or clinical characteristic, compared to cluster 1. Odds ratios and 95% confidence intervals (CI) are shown.

For further exploratory purposes, emotional and physical symptoms that were assessed separately from the survivorship care needs survey were compared between need-

clusters. Bonferroni-corrected ANOVA pairwise comparisons were made to statistically assess the differences between clusters. Means and standard deviations, and statistical differences between the clusters compared to cluster 1, are shown. P-values smaller than .05 were considered to be statistically significant.

RESULTS

The 292 patients that were included in the current study had an average age of 58.6 years, the majority was female (67%), of white race (91%), of high income (59%) and not currently on treatment (59%). The most common cancer types were breast (34%), hematologic (23%) and gastro-intestinal (11%). Participants completed the survey on average 3.7 years after the most recent cancer diagnosis (Table 1).

In our latent class cluster analysis, the four-cluster model was shown to have the best model fit, based on goodness-of-fit-statistics (Akaike's Information Criterion [AIC]; Consistent Akaike's Information Criterion [CAIC]; Table 2). Although the more conventional Bayes' Information Criterion (BIC) shows that the two cluster model has best model fit, we feel that the more liberal four-cluster model best describes variation in survivorship care needs in our sample. This model identified four clusters of survivors, including 1) low needs (N=123, 42%), 2) mainly physical needs (N=46, 16%), 3) mainly psychological needs (N=57, 20%) and 4) both physical and psychological needs (N=66, 23%; Figure 1). Among those with low needs (cluster 1), 77 survivors (26% of total) reported no needs on any domain.

Baseline characteristics significantly differed across clusters with respect to age (continuous and categorical; P<0.01), employment (P=0.05) and genito-urinary cancer type (P=0.03) (Table 3). Multiple logistic regression analysis showed that survivors with mainly physical needs (cluster 2), mainly psychological needs (cluster 3) and both physical and psychological needs (cluster 4) were younger compared to survivors with low needs (cluster 1), independent of income, education, employment or being currently on treatment (continuous age per 10 years, ORs 0.70, 0.72, 0.72; p<0.03; Table 4).

Table 1: survivor characteristics

	Total sample (N=292)
Age, M (SD)	58.6 (16.6)
Gender, N (%)	
Male	92 (33)
Female	190 (67)
Race	
White	266 (91)
Non-white	26 (9)
Educational level[a], N (%)	
low	52 (18)
medium	136 (47)
high	102 (35)
Income[b], N (%)	
low	36 (15)
medium	64 (27)
high	141 (59)
Partner/married, N (%)	214 (73)
Employed, N (%)	147 (50)
Internet access, N (%)	263 (95)
Cancer type	
Breast, N (%)	98 (34)
Gynecologic, N (%)	30 (10)
Neurologic, N (%)	3 (1)
Gastro-intestinal, N (%)	32 (11)
Genito-urinary, N (%)	22 (8)
Thoracic, N (%)	12 (4)
Head & neck, N (%)	16 (5)
Melanoma, N (%)	17 (6)
Sarcoma, N (%)	8 (3)
Hematologic, N (%)	66 (23)
Treatments received	
Surgery, N (%)	150 (51)
Chemotherapy, N (%)	208 (71)
Radiotherapy, N (%)	205 (70)
Currently on treatment, N (%)	119 (41)
Years since last diagnosis, M (SD)	3.7 (4.7)
Comorbidities[c], N (%)	
0	168 (58)
1	72 (25)
>1	53 (18)

[a]low=completed high school or lower, medium=2 years college or college graduate, high=masters or doctoral. [b]annual household income: low=<$40,000, medium=$40,000 - $80,000, high=>$80,000. [c]based on disease categories (diabetes, kidney disease, overweight/obesity, underweight, liver disease, lung disease and heart disease)

Table 2: Goodness of fit indexes for cluster models

Model	L^2 statistic	L^2 statistic p-value	BIC_{LL}	AIC_{LL}	AIC^3_{LL}	$CAIC_{LL}$
One cluster	666.66	<0.01	2660.67	2634.93	2641.93	2667.67
Two cluster	155.68	<0.01	2195.10	2139.95	2154.95	2210.10
Three cluster	113.85	0.03	2198.68	2114.12	2137.12	2221.68
Four cluster	**90.71**	**0.63**	**2220.96**	**2106.98**	**2137.98**	**2137.98**
Five cluster	81.29	0.73	2256.95	2113.56	2152.56	2295.95
Six cluster	71.97	0.79	2293.05	2120.24	2167.24	2340.05

AIC: Akaike's Information Criterion; BIC: Bayes' Information Criterion; CAIC: Consistent Akaike's Information Criterion; LL: log-likelihood. The model with the most optimal fit is in bold.

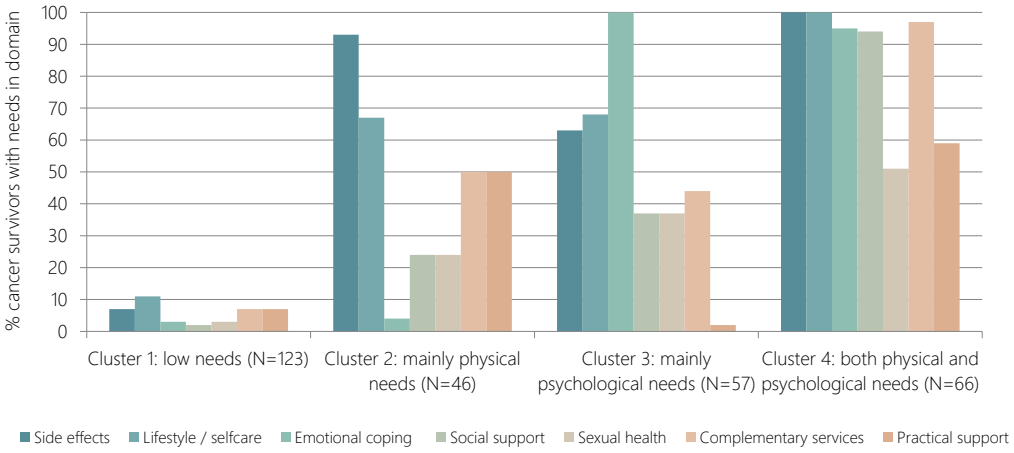


Figure 1: distribution of survivorship care needs across domains, per needs-cluster

Emotional and physical issues that were assessed in a distinct section of the survey from the needs assessment questions, were associated with the needs clusters. Emotional issues , including fear of recurrence, depression, anxiety, and insomnia, were more prevalent among survivors with mainly psychological needs (cluster 3) and with both physical and psychological needs (cluster 4), compared to low needs (cluster 1; P <0.05). Fatigue was more prevalent among survivors in clusters with mainly physical needs (cluster 2) and with both physical and psychological needs (cluster 4) compared to low needs (cluster 1; P<0.05; Figure 2).

Overall, survivors reported the highest unmet needs regarding side effects (53%), self-care (51%) and emotional coping (43%) domains. Needs related to side effects were highest for fatigue (30%), memory problems (20%) and weight gain (20%); needs related to self-care were highest for diet/nutrition counselling (34%), physical activity (30%) and meditation/relaxation (30%); and needs related to emotional coping were highest for fear of recurrence (34%), anxiety or worry (28%) and managing stress (22%; Appendix I).

Table 3: survivor characteristics per needs-cluster

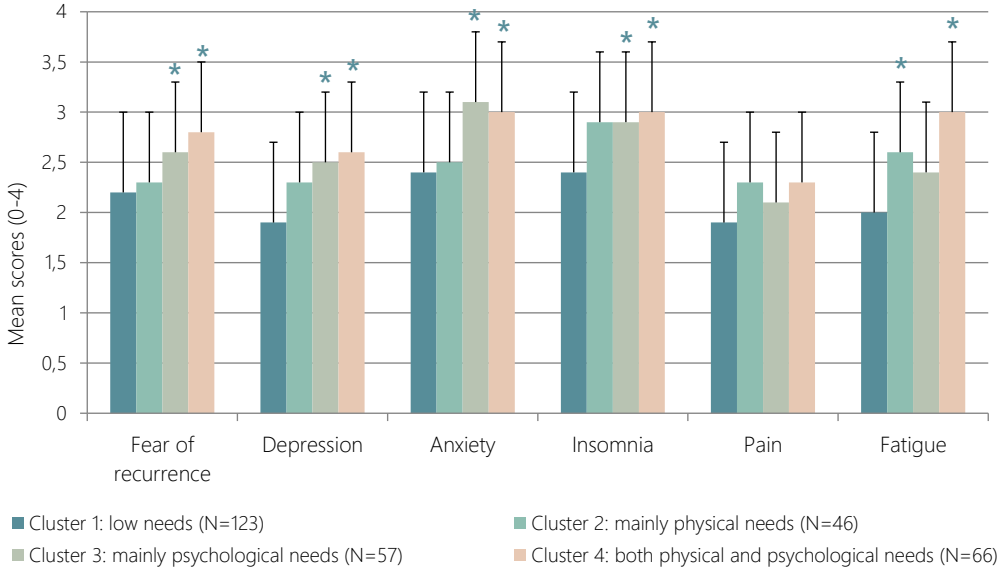
	Cluster 1: Low needs (N=123)	Cluster 2: Mainly physical needs (N=46)	Cluster 3: Mainly psychological needs (N=57)	Cluster 4: Both physical and psychological needs (N=66)	P-value*
Age, M (SD)	61.9 (12.5)	58.0 (15.1)	55.8 (12.2)	55.4 (1.4)	**<0.01**
Age categories, N (%)					
<50	17 (14)	12 (26)	15 (27)	22 (34)	
50-59	34 (29)	12 (26)	21 (38)	12 (18)	
60-69	33 (27)	10 (22)	14 (25)	24 (37)	
>70	38 (31)	12 (26)	6 (11)	7 (11)	**<0.01**
Gender, N (%)					
Male	44 (37)	16 (36)	16 (29)	16 (25)	
Female	75 (63)	28 (64)	40 (71)	47 (75)	0.36
Race					
White	113 (92)	41 (89)	54 (95)	58 (88)	
Non-white	10 (8)	5 (11)	3 (5)	8 (31)	0.56
Educational level[a], N (%)					
low	28 (23)	8 (17)	5 (9)	11 (17)	
medium	59 (48)	24 (52)	29 (51)	24 (37)	
high	35 (29)	14 (30)	23 (40)	30 (46)	0.10
Income[b], N (%)					
low	21 (21)	7 (16)	3 (7)	5 (9)	
medium	18 (18)	15 (35)	16 (35)	15 (28)	0.39
high	59 (60)	21 (49)	27 (59)	34 (62)	0.06
Partner/married, N (%)	90 (73)	36 (78)	44 (77)	44 (67)	0.47
Employed, N (%)	56 (45)	18 (39)	35 (61)	38 (58)	**0.05**
Internet access, N (%)	107 (93)	42 (95)	52 (96)	62 (97)	0.66
Cancer type					
Breast, N (%)	37 (30)	16 (35)	18 (32)	27 (41)	0.49
Gynecologic, N (%)	15 (12)	4 (9)	8 (14)	3 (5)	0.28
Neurologic, N (%)	2 (2)	0 (0)	1 (2)	0 (0)	0.60
Gastro-intestinal, N (%)	14 (11)	6 (13)	4 (7)	8 (12)	0.75
Genito-urinary, N (%)	16 (13)	2 (4)	2 (4)	2 (3)	**0.03**
Thoracic, N (%)	6 (5)	3 (7)	1 (2)	2 (3)	0.60
Head & neck, N (%)	7 (7)	3 (7)	1 (2)	5 (8)	0.53
Melanoma, N (%)	6 (5)	2 (4)	4 (7)	5 (8)	0.83
Sarcoma, N (%)	1 (1)	2 (4)	1 (2)	4 (6)	0.16
Hematologic, N (%)	29 (24)	7 (15)	17 (30)	13 (20)	0.32
Treatments received					
Surgery, N (%)	85 (69)	29 (63)	40 (70)	51 (77)	0.43
Chemotherapy, N (%)	82 (67)	35 (76)	40 (70)	51 (77)	0.39
Radiotherapy, N (%)	59 (48)	26 (57)	30 (53)	35 (53)	0.76
Currently on treatment, N (%)	40 (32)	21 (46)	25 (44)	33 (50)	0.09
Years since last diagnosis, M (SD)	4.0 (4.8)	3.4 (5.4)	4.3 (4.8)	3.1 (4.0)	0.50
Comorbidities[c], N (%)					
0	73 (59)	27 (59)	36 (63)	32 (48)	
1	29 (24)	11 (24)	9 (16)	23 (35)	
>1	21 (17)	8 (17)	12 (21)	11 (17)	0.38

Note of table 3:*p-value indicates differences between any of the clusters in Chi^2-tests or ANOVA (Bonferroni corrected). [a]low=completed high school or lower, medium=2 years college or college graduate, high=masters or doctoral. [b]annual household income: low=<$40,000, medium=$40,000 - $80,000, high=>$80,000. [c]based on disease categories (diabetes, kidney disease, overweight/obesity, underweight, liver disease, lung disease and heart disease)

Table 4: multiple logistic regression analysis of socio-demographic and clinical factors associated with clusters

	Cluster 1: Low needs (N=123)	Cluster 2: Mainly physical needs (N=46)	Cluster 3: Mainly psychological needs (N=57)	Cluster 4: Both physical and psychological needs (N=66)
		UNIVARIATE		
Age, per 10 years	1.00 (REF)	0.79 (0.61-1.03)	**0.70 (0.55-0.89)****	**0.69 (0.55-0.87)****
Education, low[a]	1.00 (REF)	0.71 (0.30-1.71)	**0.33 (0.12-0.90)***	0.68 (0.31-1.47)
Income, low[b]	1.00 (REF)	0.87 (0.34-2.21)	**0.27 (0.08-0.95)***	0.40 (0.14-1.11)
Employed	1.00 (REF)	0.77 (0.39-1.53)	1.90 (1.00-3.61)	1.62 (0.89-2.97)
Currently on treatment	1.00 (REF)	1.74 (0.87-3.48)	1.62 (0.85-3.09)	2.08 (1.13-3.83)
		MULTIVARIATE		
Age, per 10 years	1.00 (REF)	**0.70 (0.53-0.92)****	**0.72 (0.54-0.96)***	**0.72 (0.54-0.97)***
Education, low[a]	1.00 (REF)	0.96 (0.43-2.32)	0.48 (0.17-1.39)	0.77 (0.30-2.00)
Income, low[b]	1.00 (REF)	0.34 (0.11-1.05)	0.32 (0.08-1.20)	0.74 (0.26-2.11)
Employed	1.00 (REF)	0.94 (0.47-1.91)	1.07 (0.51-2.24)	0.47 (0.21-1.05)
Currently on treatment	1.00 (REF)	1.83 (0.96-3.48)	1.41 (0.71-2.78)	1.53 (0.74-3.14)

Note: only variables that differed across clusters (p≤0.1, table 1) were included. [a]completed high school or lower. [B]annual household income <$40,000.



*indicates a significant difference (p<0.05) compared to cluster 1, in ANOVA post-hoc analysis (Bonferroni corrected). Error bars show +1 standard deviation.

Figure 2: mean scores of emotional and physical symptoms across clusters

DISCUSSION

We demonstrate that the unmet needs of cancer survivors who participated in this study are indeed heterogeneous. Interestingly, our analysis suggests that over 40% of survivors report no or low unmet needs for survivorship care. For others who reported needs, we show that they may be broken down into separate subgroups: those with a) primarily physical needs related to chronic or late effects of cancer or cancer therapy, b) primarily psychological needs, and c) those with both physical and psychological unmet needs.

The identification of these subgroups and sociodemographic and clinical predictors of each subgroup does not diminish the need to screen each individual patient for survivorship care needs. It does however, provide clinical insight into how programs to address the needs of diverse survivors might be structured, and it underscores the importance of both tailored information provision and accounting for differences in needs when testing interventions in survivorship care research.

Overall, unmet survivorship care needs were highest regarding side-effects, followed by self-care and emotional coping domains. This is in line with earlier studies using other surveys, including the Supportive Care Needs Survey (SCNS),[22] and the Cancer Survivors Unmet Needs measure (CaSUN),[23] that reported the importance of psychological issues such as anxiety and fear of recurrence, information on things to do to get well, and physical issues such as side-effects. [3-5]. Our study demonstrates that needs within these domains do not always occur together and that high needs in all areas simultaneously is uncommon. Our findings are consistent with a similar cluster analysis in a population of breast cancer survivors that characterized an even greater 63% of patients within a 'few-needs' cluster. [24] This suggests that one of the goals for cancer survivorship programs could be to screen for patients' needs (or lack thereof) and then triage individuals to services focused on management of their specific issues, rather than trying to develop a single program to address all needs.

In line with previous research,[25-27] older age was associated with lower unmet survivorship care needs as compared to their younger counterparts, suggesting that more effort is needed to identify and address the needs of younger cancer survivors. Previous work suggests that younger patients experience a greater impact of the cancer and treatments on functioning and psychological wellbeing [28,29] and have higher expectations of services and people around them than older patients [30,31], while older patients show better adjustment to cancer.[32] Resilience among older patients has been explained by more experience with coping with challenging events throughout life.[33] We did not find substantial differences in cancer type across clusters, except that survivors with a genito-urinary cancer had more often low or no needs compared to the other cancer types, probably because of older

average age (68 years). Other clinical factors, such as treatment type, being currently on treatment, and time since diagnosis were not associated with need patterns in our study. Possibly, statistical power was too low to detect these associations, due to relatively small cluster sizes.

Consistent with previous literature, physical and psychological problems were associated with higher unmet needs.[34] Specifically, patients reporting current psychological issues, including fear of recurrence, depression, anxiety and, interestingly, those with insomnia were more likely to identify needs for care and information related specifically to coping or across all care domains. Patients reporting current physical issues, such as fatigue, were more likely to report needs for care and information related to management of chronic and late effects of disease and treatment, or needs across all care domains. These associations are not surprising, but it is important to note that these were distinct questions in different sections of our survey, the former focused on current symptoms or problems and the latter on patients' reported needs for assistance in care. Although we feel that further research is needed to confirm associations with need clusters using validated questionnaires measuring physical and psychological symptoms, our findings may suggest that screening for current symptoms and problems, as advocated by the National Comprehensive Cancer Network (NCCN) survivorship guideline panel, can be an effective way of identifying patients' needs for survivorship care.[35] This is also consistent with recent efforts to integrate patient-reported outcome measures (PROMs) into survivorship care pathways.[36]

Limitations

This is a single institution study, conducted primarily at an urban academic medical center serving a population with relatively high socio-economic status (SES). Due to the pragmatic nature of offering this survey across the cancer center we cannot determine response rates, making it more difficult to assess selection bias. Although this study includes a broad range of patients with regard to age and cancer type, it is possible that patients with higher symptom burden or care needs, may have been more motivated to complete the survey and may be overrepresented in our sample.[37] However, alternatively, patients with higher symptom burden may have been too stressed or fatigued to complete the questionnaire and are therefore underrepresented in our sample. Further, resources precluded translation of the survey into Arabic, Cantonese, French, Mandarin, Spanish, and Russian, which are spoken by a minority of patients at our center. Needs may differ among non-English speaking patients, and in particular there may be greater barriers related to access to care and practical assistance faced by these patients who for pragmatic reasons are not included in our sample. Nevertheless, even in a selective sample of cancer survivors, there were variations in survivorship care needs and meaningful clusters of needs among this population. These patterns may be more pronounced in a

more diverse sample. Further, a larger sample size could increase the number of clusters to be identified, which allows for assessment of need patterns in more detail.

Our study is cross-sectional and did not account for changes in survivorship care needs over time. While time from diagnosis was not associated with need-clusters, individual patterns of survivorship care needs may not be static. Repeated evaluations of survivorship care needs could elucidate the degree to which individual survivors have changing needs over time. In addition, we included all patients with curable disease, including those who were on intravenous therapy, consistent with the survivorship definition from the National Coalition for Cancer Survivors and endorsed by the American Society of Clinical Oncology which begins at diagnosis.[38] This definition mirrors the work of Dr. Mullan who recognized different phases of survivorship.[39] Needs are expected to vary based on specific regimens, time of assessment within a given regimen or from completion of therapy, as well as by use of any long term/maintenance therapies. A growing number of extended oral, intramuscular and intravenous therapies that can extend for years, now blurs the lines of completion of initial therapy and precludes a simple definition of survivorship. We chose to use a broad definition, and to be inclusive of curable patients in our analysis to mirror the pragmatic challenges of clinical practice, when needs must be assessed and addressed across this continuum. Needs for individual patients clearly do change over time depending on changes in therapy and many other factors.

We used primarily study specific survey questions. Although scales of need within domains showed good internal consistently, we cannot assure that constructs of domains were fully captured using our questionnaire. This survey relied on patient reported clinical data, not chart review, and we did not feel that determination of detailed staging information was possible.

Future directions

Because of increasing healthcare costs and limited resources for survivorship care, there is a need for efficient provision of information, interventions and care to cancer survivors. The classification of survivors into clusters based on survivorship care needs is a novel way to assess patterns of needs across survivors, in contrast to a body of literature focusing on associations with the number of needs or individual domains[3]. To our knowledge, this is the first study that assessed clusters of needs on multiple domains among patients with multiple types of cancer.

Our study demonstrates that the majority of patients (58%) do have substantial needs, even years after diagnosis, and these patients need to be identified through careful screening in follow-up care. However, we also found that a large group of cancer survivors (42%) report relatively few symptoms or problems after cancer diagnosis and identify few

care and informational needs. These patients still need quality cancer follow-up care, screening for late effects and recurrence and ongoing assessment of needs, but they do not appear to need intensive survivorship care resources. Consequently, our study may provide an explanation for the failure of some survivorship interventions, such as SCPs, to improve outcomes in randomized trials.[9-12] The impact of these interventions may be diluted by a substantial subgroup of survivors with few or no needs. In future research, interventional studies should consider identifying patients with documented needs and seeking to improve outcomes, rather than delivering an intervention to an unselected population of cancer survivors. In this respect, survivorship care interventions may need to be tested with the same rigor applied to precision cancer therapy, with the right intervention for the right patient at the right time.

We feel the needs clusters identified in our study merit validation using other needs assessment tools and across more diverse populations of patients with cancer. However, the characterization of patients as having few needs, predominantly physical needs, predominantly psychological needs, or substantial both physical and psychological needs provides a productive framework for clinical care of cancer survivors and to guide further research in this field. Further research is needed to define the tailored information and services appropriate for each group of patients, and to define optimal screening tools to efficiently identify the needs of individuals in oncology practice.

APPENDIX I

Survivorship care needs across clusters

N, (%)	Total (N=292)	Cluster 1: Low needs (N=123)	Cluster 2: Mainly physical needs (N=46)	Cluster 3: Mainly psychological needs (N=57)	Cluster 4: Both physical and psychological needs (N=66)
Side effects, total	154 (53)	9 (7)	43 (93)	36 (63)	66 (100)
Pain	46 (16)	3 (2)	11 (24)	5 (9)	27 (41)
Fatigue	87 (30)	6 (5)	17 (37)	20 (35)	44 (67)
Hot flashes	49 (17)	2 (2)	11 (24)	13 (23)	23 (35)
Lymphedema/swelling	34 (12)	4 (3)	6 (13)	4 (7)	20 (30)
Osteoporosis/bone health	35 (12)	2 (2)	7 (15)	5 (9)	21 (32)
Nausea/vomiting	23 (8)	3 (2)	2 (4)	4 (7)	14 (21)
Trouble swallowing	18 (6)	3 (2)	4 (9)	2 (4)	9 (14)
Dental or mouth problems	28 (10)	2 (2)	7 (15)	4 (7)	15 (23)
Diarrhea or constipation	40 (14)	3 (2)	8 (17)	8 (14)	21 (32)
Bowel or bladder changes	32 (11)	3 (2)	5 (11)	8 (14)	17 (26)
Memory problems	59 (20)	2 (2)	11 (24)	12 (21)	34 (52)
Concentration difficulties	58 (20)	2 (2)	7 (15)	16 (28)	33 (50)
Body changes	40 (14)	2 (2)	3 (7)	10 (18)	25 (38)
Hair and skin care changes	47 (16)	4 (3)	8 (17)	5 (9)	30 (45)
Coordination	29 (10)	2 (2)	2 (4)	5 (9)	20 (30)
Weight gain	57 (20)	3 (2)	13 (28)	9 (16)	32 (48)
Weight loss	28 (10)	3 (2)	4 (9)	3 (5)	18 (27)
Lifestyle/ self-care, total	149 (51)	13 (11)	31 (67)	39 (68)	66 (100)
Diet/nutrition counseling	98 (34)	9 (7)	19 (39)	20 (35)	51 (77)
Physical activity	89 (30)	7 (6)	16 (35)	16 (28)	50 (76)
Sleep specialist	67 (23)	0 (0)	15 (33)	19 (33)	33 (50)
Weight center	61 (21)	3 (2)	9 (20)	11 (19)	38 (58)
Tobacco treatment	5 (2)	0 (0)	0 (0)	1 (2)	4 (6)
Meditation/ relaxation	88 (30)	7 (6)	11 (24)	20 (35)	50 (76)
Emotional coping, total	126 (43)	4 (3)	2 (4)	57 (100)	63 (95)
Anger	28 (10)	0 (0)	0 (0)	9 (16)	19 (29)
Grief or loss	34 (12)	0 (0)	0 (0)	9 (16)	25 (38)
Sadness	49 (17)	1 (1)	0 (0)	16 (28)	32 (48)
Anxiety or worry	83 (28)	2 (2)	0 (0)	36 (63)	45 (68)
Fear of cancer recurrence	100 (34)	2 (2)	2 (4)	46 (81)	50 (76)
Managing stress	63 (22)	0 (0)	0 (0)	26 (46)	37 (56)
End of life	33 (11)	0 (0)	1 (2)	10 (18)	22 (33)
Feeling alone	35 (12)	1 (1)	1 (2)	10 (19)	23 (25)

N, (%)	Total (N=292)	Cluster 1: Low needs (N=123)	Cluster 2: Mainly physical needs (N=46)	Cluster 3: Mainly psychological needs (N=57)	Cluster 4: Both physical and psychological needs (N=66)
Complementary services, total	121 (41)	9 (7)	23 (50)	25 (44)	64 (97)
Counseling	35 (12)	1 (1)	2 (4)	8 (14)	24 (36)
Music therapy	34 (12)	0 (0)	7 (15)	2 (4)	25 (38)
Art therapy	26 (9)	0 (0)	6 (13)	2 (4)	18 (27)
Pain clinic	19 (7)	0 (0)	4 (9)	1 (2)	14 (21)
Chaplain/spiritual counseling	21 (7)	0 (0)	2 (4)	2 (4)	17 (26)
Social work	17 (6)	0 (0)	0 (0)	2 (4)	15 (23)
Acupuncture	55 (19)	3 (2)	10 (22)	8 (14)	34 (52)
Chiropractor	29 (10)	1 (1)	6 (13)	4 (7)	18 (27)
Hypnosis	19 (7)	0 (0)	2 (4)	1 (2)	16 (24)
Yoga/Tai Chi/Qi gong	65 (22)	4 (3)	10 (22)	13 (23)	38 (58)
Physical therapy	42 (14)	2 (2)	5 (11)	7 (12)	28 (42)
Massage therapy	82 (28)	2 (2)	13 (28)	15 (26)	52 (79)
Energy Healing	60 (21)	1 (1)	8 (17)	11 (19)	40 (61)
Herbal Supplements	58 (20)	5 (4)	14 (30)	9 (16)	30 (45)
Social support, total	97 (33)	3 (2)	11 (24)	21 (37)	62 (94)
Meeting others with cancer	39 (19)	1 (1)	3 (7)	6 (11)	29 (44)
Peer support group	44 (15)	1 (1)	3 (7)	8 (14)	32 (49)
Social activities	25 (9)	1 (1)	3 (7)	3 (4)	19 (29)
Retreats/camps	24 (8)	1 (1)	1 (2)	2 (4)	20 (30)
Talking	26 (9)	1 (1)	0 (0)	5 (9)	20 (30)
Giveback/volunteer	51 (17)	3 (2)	3 (7)	9 (16)	26 (55)
Return to work	33 (11)	0 (0)	3 (7)	5 (9)	25 (38)
Religious/ spiritual support	18 (6)	0 (0)	0 (0)	1 (2)	17 (26)
Finding support children	36 (12)	0 (0)	3 (7)	6 (11)	27 (41)
Finding support caregiver	30 (10)	0 (0)	3 (7)	4 (7)	23 (35)
Finding support family	32 (11)	0 (0)	2 (4)	6 (11)	24 (36)
Sexual health, total	70 (24)	4 (3)	11 (24)	21 (37)	34 (51)
Sexual issues	48 (16)	3 (2)	8 (17)	14 (25)	23 (35)
Fertility issues	15 (5)	1 (1)	1 (2)	3 (5)	10 (15)
Body image concerns	34 (12)	0 (0)	4 (9)	10 (18)	20 (30)
Intimacy concerns	35 (12)	1 (1)	4 (9)	9 (16)	21 (32)
Practical support, total	71 (24)	8 (7)	23 (50)	1 (2)	39 (59)
Finding PCP	17 (6)	0 (0)	3 (7)	1 (2)	13 (20)
Transitioning care	9 (3)	0 (0)	1 (2)	0 (0)	8 (12)
Childcare	8 (3)	0 (0)	2 (4)	1 (2)	5 (8)
Financial counseling	23 (8)	0 (0)	6 (13)	1 (2)	16 (24)
Assistance paying	19 (7)	1 (1)	5 (11)	0 (0)	13 (20)
Insurance questions	29 (10)	1 (1)	7 (15)	0 (0)	21 (32)

REFERENCES

1. Miller K, Siegel R, Lin C, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016;66(4):271-289.
2. Aaronson NK, Mattioli V, Minton O, et al. Beyond treatment–psychosocial and behavioural issues in cancer survivorship research and practice. *European Journal of Cancer Supplements.* 2014;12(1):54-64.
3. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Supportive Care in Cancer.* 2009;17(8):1117-1128.
4. Geller BM, Vacek PM, Flynn BS, Lord K, Cranmer D. What are cancer survivors' needs and how well are they being met? *The Journal of family practice.* Oct 2014;63(10):E7-16.
5. Kent EE, Arora NK, Rowland JH, et al. Health information needs and health-related quality of life in a diverse population of long-term cancer survivors. *Patient education and counseling.* 2012;89(2):345-352.
6. Mayer DK, Nasso SF, Earp JA. Defining cancer survivors, their needs, and perspectives on survivorship health care in the USA. *The Lancet. Oncology.* Jan 2017;18(1):e11-e18.
7. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
8. Page AE, Adler NE. *Cancer care for the whole patient: Meeting psychosocial health needs*. National Academies Press; 2008.
9. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
10. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
11. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment.* 2013;138(3):795-806.
12. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
13. Birken SA, Mayer DK, Weiner BJ. Survivorship care plans: prevalence and barriers to use. *Journal of cancer education : the official journal of the American Association for Cancer Education.* Jun 2013;28(2):290-296.
14. Stricker CT, Jacobs LA, Risendal B, et al. Survivorship care planning after the institute of medicine recommendations: how are we faring? *Journal of cancer survivorship : research and practice.* Dec 2011;5(4):358-370.
15. Salz T, McCabe MS, Onstad EE, et al. Survivorship care plans: is there buy-in from community oncology providers? *Cancer.* Mar 01 2014;120(5):722-730.
16. Maly RC, Liang L-J, Liu Y, Griggs JJ, Ganz PA. Randomized Controlled Trial of Survivorship Care Plans Among Low-Income, Predominantly Latina Breast Cancer Survivors. *Journal of Clinical Oncology.* 2017;35(16):1814-1821.
17. Nekhlyudov L, Ganz PA, Arora NK, Rowland JH. Going Beyond Being Lost in Transition: A Decade of Progress in Cancer Survivorship. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jun 20 2017;35(18):1978-1981.
18. Parry C, Kent EE, Forsythe LP, Alfano CM, Rowland JH. Can't see the forest for the care plan: a call to revisit the context of care planning. *Journal of Clinical Oncology.* 2013;31(21):2651-2653.
19. Gotay CC, Pagano IS. Assessment of Survivor Concerns (ASC): a newly proposed brief questionnaire. *Health Qual Life Outcomes.* Mar 13 2007;5:15.
20. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Mar 1993;11(3):570-579.

21. Vermunt JK, Magidson J. *Latent GOLD 4.0 User's Guide*. Belmont, Massachusetts: Statistical Innovations Inc2005.
22. Boyes A, Girgis A, Lecathelinais C. Brief assessment of adult cancer patients' perceived needs: development and validation of the 34-item Supportive Care Needs Survey (SCNS-SF34). *J Eval Clin Pract*. Aug 2009;15(4):602-606.
23. Hodgkinson K, Butow P, Hunt GE, et al. The development and evaluation of a measure to assess cancer survivors' unmet supportive care needs: the CaSUN (Cancer Survivors' Unmet Needs measure). *Psycho-oncology*. Sep 2007;16(9):796-804.
24. Aranda S, Schofield P, Weih L, et al. Mapping the quality of life and unmet needs of urban women with metastatic breast cancer. *European journal of cancer care*. 2005;14(3):211-222.
25. Barg FK, Cronholm PF, Straton JB, et al. Unmet psychosocial needs of Pennsylvanians with cancer: 1986–2005. *Cancer*. 2007;110(3):631-639.
26. Sanson-Fisher R, Girgis A, Boyes A, Bonevski B, Burton L, Cook P. The unmet supportive care needs of patients with cancer. *Cancer*. 2000;88(1):226-237.
27. Soothill K, Morris S, Harman J, Francis B, Thomas C, McIllmurray M. The significant unmet needs of cancer patients: probing psychosocial concerns. *Supportive care in Cancer*. 2001;9(8):597-605.
28. Ganz PA, Schag CC, Heinrich RL. The psychosocial impact of cancer on the elderly: a comparison with younger patients. *Journal of the American Geriatrics Society*. 1985;33(6):429-435.
29. Kroenke CH, Rosner B, Chen WY, Kawachi I, Colditz GA, Holmes MD. Functional impact of breast cancer by age at diagnosis. *Journal of Clinical Oncology*. 2004;22(10):1849-1856.
30. Sitzia J, Wood N. Patient satisfaction: a review of issues and concepts. *Social science & medicine*. 1997;45(12):1829-1843.
31. Thompson AG, Sunol R. Expectations as determinants of patient satisfaction: concepts, theory and evidence. *International journal for quality in health care*. 1995;7(2):127-141.
32. Cohen M, Baziliansky S, Beny A. The association of resilience and age in individuals with colorectal cancer: an exploratory cross-sectional study. *Journal of geriatric oncology*. 2014;5(1):33-39.
33. Brandtstädter J. Sources of resilience in the aging self: Toward integrating perspectives. *Social cognition and aging*: Elsevier; 1999:123-141.
34. Hodgkinson K, Butow P, Hunt GE, Pendlebury S, Hobbs KM, Wain G. Breast cancer survivors' supportive care needs 2-10 years after diagnosis. *Supportive care in cancer : official journal of the Multinational Association of Supportive Care in Cancer*. May 2007;15(5):515-523.
35. Denlinger CS, Ligibel JA, Are M, et al. Survivorship: screening for cancer and treatment effects, version 2.2014. *Journal of the National Comprehensive Cancer Network*. 2014;12(11):1526-1531.
36. Warrington L, Absolom K, Velikova G. Integrated care pathways for cancer survivors - a role for patient-reported outcome measures and health informatics. *Acta oncologica (Stockholm, Sweden)*. May 2015;54(5):600-608.
37. Paganini-Hill A, Hsu G, Chao A, Ross RK. Comparison of early and late respondents to a postal health survey questionnaire. *Epidemiology*. 1993:375-379.
38. McCabe MS, Bhatia S, Oeffinger KC, et al. American Society of Clinical Oncology statement: achieving high-quality cancer survivorship care. *Journal of Clinical Oncology*. 2013;31(5):631-640.
39. Mullan F. Seasons of survival: reflections of a physician with cancer. Mass Medical Soc; 1985.

Chapter 8

Survivorship care planning in gynecologic oncology – perspectives from patients, caregivers and health care providers

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ABSTRACT

Purpose: This qualitative study sought to describe the challenges following treatment and the preferences regarding survivorship care among patients treated for gynecological cancer, their caregivers and health care providers.

Methods: Between July and August 2017, in-depth semi-structured interviews regarding survivorship were conducted at a large academic hospital in the United States among patients who recently completed treatment (<12 months) for a gynecological cancer (ovarian, endometrial, cervical and vulvar) and their primary caregivers. A focus group was conducted among health care providers (oncologists, nurses and fellows). Main themes were identified using descriptive content analysis.

Results: A total of 30 individuals participated in this study (13 patients, 9 caregivers, 8 health care providers). Almost all participants reported a desire for more information on how to address survivorship needs, specifically as they related to side effects, follow-up schedule, and psychological assistance. Despite this uniformly identified need for more information, preferences for survivorship care planning differed across cancer types and individuals, with respect to content, timing and mode of delivery. Health care providers expressed challenges in communicating with patients about survivorship, a desire to shift post-treatment conversations to the goal of improving quality of life as opposed to focusing on disease recurrence, and an unmet need for disease specific and individualized survivorship care planning.

Conclusions: Patients, caregivers and health care providers each expressed a need for gynecologic cancer-tailored survivorship care resources.

Implications for cancer survivors: The variation of disease types and patient and caregiver needs may require multi-faceted, individualized survivorship care planning.

INTRODUCTION

Each year, almost 106,000 women in the United States are diagnosed with a gynecological cancer.[1] Ovarian cancer remains the deadliest gynecological cancer, followed by vaginal, cervical, endometrial and vulvar cancer. The estimated five-year survival rates vary widely from 46% for women with ovarian cancer to over 80% for women with endometrial or vulvar malignancies.[1] Survival rates for gynecological cancers have slightly increased during the past decades,[1] reflecting advances in treatment that ultimately help patients survive their disease.

Regardless of prognosis, a wide body of literature supports the notion that women treated for gynecological cancer experience a significant level of disease- and treatment-related symptoms that persist after the end of first-line treatment and greatly impact their long-term quality of life.[2-7] In addition, one of the most significant and overwhelming psychological concerns cancer survivors struggle to manage is the fear of cancer recurrence, which is associated with increased symptom burden, overwhelming anxiety, post-traumatic stress, and hopelessness.[4,6,8-10]

The National Academy of Medicine (NAM) acknowledged that these factors are important in the ongoing care for cancer patients ending treatment, and in 2006 recommended that all cancer survivors receive a Survivorship Care Plan (SCP).[11] SCPs typically contain written information on diagnosis, documentation of all treatments, short- and long term effects of the treatments, and recommendation for follow-up care.[11] To date, multiple randomized controlled trials evaluating the impact of SCPs among cancer patients,[12-17] including gynecological cancer,[13,16,18] have failed to demonstrate beneficial effects of SCPs on short or long-term satisfaction with information provision and care, quality of life or distress. These outcomes suggest that patients with gynecological cancer may not receive the intended benefits of an SCP as proposed by the NAM without further refinement and evaluation of these interventions.[19]

Part of the disconnect between the prominent calls for SCPs as a self-evident beneficial intervention and the lack on strong evidence supporting SCPs in their current format may stem from a failure to adequately tailor these interventions to the needs of specific cancer patient populations. Additionally, there may be a need to further adapt the intervention to the needs and preferences of the individual patient. Given the lack of evidence to support existing SCP models in the setting of gynecologic oncology, we sought to describe the perspectives of patients with gynecological cancer, as well as their caregivers and health care providers (HCPs). This may provide insights into the unmet needs of patients and their caregivers as well as challenges to the healthcare team and identify opportunities for effective intervention through SCPs or other aspects of survivorship care.

The aim of the current study is to describe the 1) challenges following treatment and 2) the preferences regarding survivorship care among patients treated for gynecological cancer, their caregivers and HCPs.

METHODS

Design

This study employed an open-ended qualitative descriptive design including in-depth semi-structured interviews among three stakeholder groups: patients with a gynecological cancer, their caregivers, and gynecologic oncology HCPs with whom we conducted a focus group. The study protocol was approved by the Dana-Farber/Harvard Cancer Center Institutional Review Board.

Participants and recruitment

Patients older than 18, able to read and respond in English, that completed treatment for any type of gynecological cancer within the past 12 months, were eligible to participate in the study. The study team reviewed upcoming clinic schedules for eligible patients and invited those patients to participate during a scheduled outpatient clinic visit at the Cancer Center, or were invited by phone. Patients were asked to identify their primary caregiver defined as a spouse, family member or friend who provides care and support to the patient. Caregivers were introduced to the study at the Cancer Center, or by phone when not present at the Cancer Center. After informed consent, telephone or in-person interviews with patients and caregivers were scheduled at a time convenient for them. HCPs that primarily provide care for patients with gynecologic cancer (gynecologic oncolgists, medical oncologists, gynecologic oncology fellows and nurse practitioners) were invited to participate in a focus group interview during a regular gynecologic oncology staff meeting. Informed consent was obtained at the beginning of the meeting.

Data collection

Telephone or in-person interviews with patients and caregivers and the HCPs focus group were digitally recorded. Audio-recordings were transcribed verbatim to text using TranscribeMe.com. In addition, demographic questionnaires were completed by patients and caregivers. Measures included age, sex, ethnicity, education and employment. Clinical patient data was extracted from each patient's electronic medical record.

Interview guide

Semi-structured qualitative interview guides were developed by members of the study team. We purposefully included open-ended questions to determine patient and caregiver needs a priori with minimal predetermined categories of survivorship care

planning topics. While the patient and caregiver questionnaire guides included similar items tailored for each group, separate questionnaire guides were developed for HCPs. The interview guides were discussed and refined by study team members resulting in a list of questions and follow-up probes for each group.

Data analysis

Data transcripts were coded in NVivo 11 (QSR International) using descriptive content analysis techniques. The initial coding scheme for patient and caregiver interviews was based on the first 3 patient interviews and iteratively refined and expanded while reviewing additional interviews. Two study researchers (THT and BHR) generated the categories independently through a close reading of the transcript texts, jointly comparing their categories, reviewing any discrepancies and disagreements, and resolving discrepancies through consensus. We continued reviewing coding until saturation was achieved and no new category themes emerged. After developing a comprehensive list of categories, we then summarized and classified the categories into higher-order themes. To ensure consistency between themes, categories, and the raw data, we selected representative quotations of each theme to illustrate its meaning and assist with data interpretation. Codebooks were developed for patient interviews first, and applied to the caregivers' interviews after determining similar content between these interviews. The HCP focus group was coded separately due to their distinct perspective and ideas discussed. We calculated the frequency of specific categories and compare these to patients' and caregivers' responses. Based on emerging categories indicating differences in type of gynecological cancer, we also decided to compare the perspectives of patients and caregivers with ovarian cancer versus other gynecological cancer types. As a qualitative study, we focused our comparisons on basic descriptive statistics and did not use our quantified data to statistically test group differences to avoid over-simplifying our qualitative exploratory data.

RESULTS

In total, we had 30 participants included in this study (thirteen patients, nine caregivers and eight HCPs). Five patients that were approached did not want to participate (no time/busy or did not want to be reminded of their cancer) and one patient was lost to follow-up. Four caregivers identified by patients chose not to participate in the study. Only one patient had an in-person interview, all other patients and caregivers preferred telephone interviews. Interviews for patient and caregiver participants lasted 30 – 40 minutes. The focus group interview of the providers was 35 minutes.

Participant characteristics

Table 1 describes patient and caregiver characteristics. Patients (n=13) represented various gynecological cancer types, including ovarian (n=5), endometrial (n=4), cervical (n=2), fallopian tube (n=1) and vulvar (n=1), had an average age of 63, were predominantly white (92%), unemployed at the time of the interview (62%) and completed treatment 6 months before the interview. Caregivers of patients (n=9) were mostly the patient's spouse (n=6), had an average age of 59, were predominantly male (78%), white (100%), and employed at the time of the interview (56%). The HCP focus group (n=8) included gynecologic oncolgists (n=2), gynecologic oncology fellows (n=3), a medical oncologist (n=1), a radiation oncologist (n=1) and a nurse practitioner, (n=1), and were predominantly female (n=5, 63%).

Perspectives of patients and caregivers

The major categories found in patient and caregiver interviews were: (1) symptoms and concerns, (2) fear of recurrence, (3) information, (4) needs, (5) satisfaction with care, (6) self-management and coping (7) preferences for survivorship care planning. Illustrative quotations are presented below and additional quotations are stated in Table 2.

Symptoms and concerns. Patient symptoms causing distress were described by the majority of both patients and caregivers (10/13 patients; 9/9 caregivers). Pain (4/13 patients; 2/9caregivers), neuropathy (3/13 patients; 2/9 caregivers), fatigue (3/13 patients, 1/9 caregivers) and anxiety/depression (2/13 patients; 4/9 caregivers) were the most commonly discussed distressing symptoms. One patient noted that managing her symptoms after treatment ended was particularly challenging:

> *"Post-treatment… that was the hardest time during the whole process because there were a multitude of side-effects that I was dealing with that … I didn't have enough information about …I just wasn't reassured enough that it was going to get better. Or maybe I was unable to absorb that it was going to get better." (Patient 11, vulvar cancer, stage unknown).*

Almost half of patients (6/13) expressed that they had limited or no post-treatment symptoms, indicating that whatever symptoms they did experience were not distressing.

While some caregivers reported a similar desire for reassurance that physical symptoms would subside post-treatment, they reported many more concerns about dealing with the emotional adjustment. For example, one caregiver described his lack of training in medical symptoms and concern about his ability to emotionally support his wife:

Table 1: patient and caregiver characteristics

	Patients			Caregivers		
	Total (N=13)	Ovarian cancer (n=6)	Non-ovarian cancer (n=7)	Total (N=9)	Ovarian cancer (n=5)	Non-ovarian cancer (n=4)
Age, M (min-max)	63.1 (48-71)	63.0 (48-71)	61.7 (51- 75)	58.7 (34-73)	60.4 (34-73)	56.5 (37-79)
Sex						
Male	0 (0)	0 (0)	0 (0)	7 (78)	4 (80)	3 (75)
Female	100 (100)	100 (100)	100 (100)	2 (22)	1 (20)	1 (25)
Ethnicity						
White	12 (92)	6 (100)	6 (86)	100 (100)	100 (100)	100 (100)
Asian	1 (8)	0 (0)	1 (14)	0 (0)	0 (0)	0 (0)
Educational level						
High school diploma or 2 year/associate's degree	3 (23)	2 (33)	1 (14)	1 (11)	1 (20)	0 (0)
4 year/ bachelor's degree	3 (23)	1 (17)	2 (28)	3 (33)	1 (20)	1 (25)
Graduate/professional degree	4 (31)	3 (50)	1 (14)	3 (33)	3 (60)	1 (25)
Unknown	3 (23)	0 (0)	3 (43)	2 (22)	0 (0)	2 (50)
Employed						
Yes	3 (23)	1 (17)	2 (28)	5 (56)	2 (40)	1 (25)
No	8 (62)	5 (83)	3 (43)	2 (22)	3 (60)	1 (25)
Unknown	2 (15)	0 (0)	2 (28)	2 (22)	0 (0)	2 (50)
Patient clinical characteristics						
Cancer type, N (%)						
Ovarian	6 (46)	6 (100)	N/A	7 (55)	5 (100)	N/A
Endometrial	4 (31)	N/A	4 (57)	1 (11)	N/A	1 (25)
Cervical	2 (15)	N/A	2 (29)	2 (22)	N/A	2 (50)
Vulvar	1 (8)	N/A	1 (14)	1 (11)	N/A	1 (25)
Cancer stage, N (%)						
I	3 (23)	0 (0)	3 (23)	0 (0)	0 (0)	0 (0)
II	4 (31)	2 (33)	2 (28)	4 (44)	2 (40)	2 (50)
III	2 (15)	3 (50)	1 (14)	1 (11)	2 (60)	0 (0)
IV	3 (23)	1 (17)	2 (28)	3 (33)	1 (20)	1 (25)
Unkown	1 (8)	0 (0)	1 (14)	1 (11)	0 (0)	1 (25)
Treatment type, N (%)						
Surgery only	2 (15)	0 (0)	2 (28)	0 (0)	0 (0)	0 (0)
Chemotherapy	6 (46)	1 (83)	1 (17)	5 (55)	4 (80)	1 (25)
Chemo + radiotherapy	5 (38)	1 (17)	4 (57)	4 (44)	1 (20)	3 (75)
Months since end of treatment, M (min-max)	6.4 (1-11)	5.2 (1-10)	7.4 (2-11)	5.9 (1-11)	8.0 (2-9)	4.2 (1-10)

Table 2: Themes identified and exemplary quotes of patients and caregivers

Theme	Description	Patients quotes	Caregivers quotes
Symptoms and concerns	Distressing symptoms (chemo brain, constipation and diarrhea, hair loss, neuropathy, nausea, pain), mood (anxiety, depression), recovering from the cancer and treatment	"A roller coaster, you're like, some days you're fine. And then other days, I get myself getting a little depressed, and anxious, and overwhelmed with the thought that I had cancer. So I don't know. Maybe they could be some sort of help in that way." (Patient 3, fallopian tube cancer, stage IIB) "In my mind, I was thinking that when chemo was done, I was going to be fine. I never experienced the side effects during my chemo but the people do. All the side effects happened at the end so-- which was bit alarming to me because I thought, well, maybe I had escaped all the side effects. But I hadn't." (Patient 7, ovarian cancer, stage IIIB)	"So the biggest concern is when is this all going to go away? When is it all going to be over and she'll just be back to normal, I guess, is the biggest concern." (Caregiver 14, cervical cancer, stage IIB) "It's very reassuring to hear them tell you what to expect and that the symptoms that she's going through are just normal and they're going to get better and it's-- that's very reassuring to hear it from somebody live than to read about it and just to get notes on it, so." (Caregiver 14, cervical cancer, stage IIB)
Fear of recurrence		"...I'd rather not dwell on something else. I don't think that's a productive use of time." (Patient 6, endometrial cancer, stage IA)	"But I suppose it's always going to be something in the back of my mind, I'm just going to think about probably more than 50% of cancer patients get it back at some point in their life. So yeah, it's, again, probably somewhat concerned. Does it affect my day-to-day life or anything like that? No." (Caregiver 4, endometrial cancer, stage IIIA; and ovarian cancer stage unknown)) "I know it is going to come back.... It affects my attitude toward my future." (Caregiver 7, ovarian cancer, stage IIIB)
Information	Wanting information on things to look out for, not wanting too much information, not wanting to be scared		"If there's anything I can do to detect the symptoms so early on, regardless of how minute or simple it may be, and how silly it might prompt a doctor's appointment, I want to know about it." (Caregiver 1, ovarian cancer, stage I) , stage IIIB)

Theme	Description	Patients quotes	Caregivers quotes
Needs	Need for information (complementary treatments, contact information/referral, follow-up plan, lifestyle, recurrence and prevention, side-effects and treating symptoms, support groups and peer support)	"Nobody's told me, so I'm assuming that everything's taken care of. And she's [oncology provider] telling me that ... it can come back. Well, where is it going to come back? What do I look for? I mean, I'm going down there every six months to be checked, what is she checking? I don't know." (Patient 2, endometrial cancer, stage IA) "I would like to stay with [cancer hospital] as part of my survivorship care. I do not choose to transition over to my primary care.... And I'm hoping that [cancer hospital] will let me do that. And my primary care, I like, but I don't have a very strong allegiance to the hospital community that they represent or that they are affiliated with. I just don't care for their quality of care." (Patient 7, ovarian cancer, stage IIIB) "I've got side effects that I'm trying to get help with, and I've got three different doctors, and I'm talking to each of the doctors, and it seems to be nobody's responsibility to assist me with these issues. I don't know the primary person that I should call. There's a definite disconnect between the doctors." (Patient 13, cervical cancer, stage IIA)	"What can we do? I know there's tons of stuff we can do to help prevent cancer. Just by eating a cleaner diet, less processed food. So I want to know about those things. Nutritional issues, supplements to help keep it from coming back, lifestyle changes. What are the signs and symptoms to look for if you're not feeling well? Is it a sign or a symptom that is going to signal something is going on again? Those things. I mean, aside from the general if you feel pain, if you have discharge, if you're bleeding. Is there something else? Maybe something more subtle?" (Caregiver 1, ovarian cancer, stage IV) "A lot of those symptoms can be symptoms of something else as well. So if you've got a backache or you've got nausea, you're tired, or whatever, it might be from cancer and it might not. So I don't know if-- probably no way to really help differentiate between what's bad and what's attributable to something else." (Caregiver 10, endometrial cancer, stage IV) "I can't really say that the team didn't say this could happen because I'm not sure that-- I don't know anything that could really prepare you for what happened and I think that what happened is-- my impression is that it just-- what happens and it can be really different all the time." (Caregiver 11, vulvar cancer, stage unknown)

Theme	Description	Patients quotes	Caregivers quotes
Satisfaction with care	Satisfaction with follow-up care, information and resources of oncology team, trust in oncology health care providers	"The other part of our conversation was about if the cancer comes back and … he assured me that, just because I am not being seen every three months, doesn't mean that they're not paying attention to my needs during this time." (Patient 8, ovarian cancer, stage IIIC) "As the treatments ended, there was a lack of understanding of what happens next. There wasn't enough information given to me. At the beginning of the treatment, there's a lot of information. This is how we all proceed. At the end of the treatment, there was no-- I was never told how often my visits would be, what I needed to look out for. It was just like last visit, and that was it. And walked away, and I was more confused at the end than I was at the beginning." (Patient 13, cervical cancer, stage IIA)	"I'm assuming that the medical profession has worked out these numbers for the first year, you do a certain thing, for the next years, you do other things, and I'm comfortable with that." (Caregiver 12, ovarian cancer, stage IIB) "I assume they go for a one-hour appointment, and they spend ten minutes. Fine if that works. But [patient] has a lot of questions. And I can always sense that the provider, very politely, is watching their watch and trying to get out of the room. Fine. This is treatment. Let's get it done. But when you get the survivorship, I would think that it would be a little better to just let the person have their half hour or hour, whatever it takes, that they're comfortable." (Caregiver 7, ovarian cancer, stage IIIB) "It's just a really poor lack of continuity in care and results. Dr. [name] didn't want to give her pain medication because he couldn't understand why she was having pain, and then she came back and then she was at [hospital] trying to get pain management. They wouldn't give her any pills, because they never saw the scans. So she kind of just ping-ponged back and forth between these two doctors, and all she wanted was pain management." (Caregiver 13, cervical cancer, stage IIA)

Theme	Description	Patients quotes	Caregivers quotes
Self-management and coping	Searching for health information online, support from others, spiritual coping, being optimistic, doing everything you can	"I would say that I'm probably more hyper-vigilant around if something doesn't feel right that I investigate." (Patient 11, vulvar cancer, stage unknown) "I just have to keep praying and be hopeful that the kind of treatment I had, (...) has worked and will give me five years cancer free. That's what I'm hoping for." (Patient 7, ovarian cancer, stage IIIB) "So I asked a lot of questions. I talked to a lot of people. I called friends that were nurses, nurse practitioners, people that have gone through it. I asked them questions. I told my family, and they contacted people." (Patient 4, endometrial cancer, stage IIIA; and ovarian cancer stage unknown)	"I want to make sure that I'm not missing anything. I know they do studies. She's already been told she can participate in studies. I want to have keen and constant awareness of what's going on in that area." (Caregiver 7, ovarian cancer, stage IIIB) "Knowing other people were going through it was very empowering, that you weren't the only one. That a lot of the things that you were feeling, they were feeling, and that there were a bunch of people trying to get through this together, as opposed to an individual." (Caregiver 3, fallopian tube, IIB) "So we used that as well as just looking stuff up on the internet. But the problem with the internet it's like anything you look up, you could look up ten sites and have ten different opinions." (Caregiver 4, endometrial cancer, stage IIIA; and ovarian cancer stage unknown)) "We'd remained pretty optimistic, given her performance and sort of focusing on the idea that the-- I think somebody has to be in the 10% that survive. And we were focusing on that. When the blood work came back that sort of blew that out of the water. So I'm sort of reassessing at this point." (Caregiver 10, endometrial cancer, stage IV)

Theme	Description	Patients quotes	Caregivers quotes
Survivorship care Planning	Preferences for survivorship care planning regarding content, mode of delivery, timing and people involved, personalized survivorship care planning	"I think it's just like if something's abnormal. I need to say something. I think it starts with me. No one's going to know unless I say something, and the doctors, I think they're pretty much on the ball, at least the ones I've worked with." (Patient 6, endometrial cancer, stage IA) "I'd like it as soon as possible, within the next six months, three months. The document would certainly be something that would be created by hopefully myself, my oncologist, and my husband. And I wouldn't mind having an infusion nurse there with us. Because the nursing staff has different perspective on things than oncologists themselves." (Patient 7, ovarian cancer, stage IIIB) "Sometimes when you're sitting in the doctor's office, which is why my husband always comes with me, I hear things differently than he might hear something or I might not hear something at all or just think it wasn't important and he will say, "Well, it was kind of important," or, "No, that wasn't really what I think the doctor meant." (Patient 14, cervical cancer, stage IIB) "Any updates in the therapies or studies that would give hope to an ovarian cancer survivor, if they could be updated on the internet and an email sent to the patient stating, 'This is what we've found, this is our most recent findings, and this is how it would impact you.'" (Patient 8, ovarian cancer, stage IIIC)	"I think that at first post-treatment appointment, [survivorship care planning] should be a conversation. And it should be on paper and then follow up with maybe an electronic version of any update, what have you." (Caregiver 1, ovarian cancer, stage IV) "I think, obviously, the patient, and hopefully, the caregiver could be there [for survivorship care planning]. And that's who should--certainly, the patient needs to receive it, and it would be nice if the caregiver got the same thing. But I still think it would be useful to be in a group setting." (Caregiver 3, fallopian tube, stage IIB) "The things that I'd like to know about are the things that are the most important things to look for. But ... I'm not sure that I would even be qualified or [patient] would be qualified to evaluate certain symptoms, right? Without real medical training." (Caregiver 11, vulvar cancer, stage unknown) "I think it should be throughout the course of treatment. Like I said, it will always probably be a snapshot of where you are in treatment and what is going on. As the treatment progresses, I imagine that some of this information will change or emphasis will be shifted." (Caregiver 12, ovarian cancer, stage IIB) "I think personalized to a certain degree. I wouldn't expect someone to go and create the [caregiver] and [patient] website. I wouldn't expect there to be someone who would go through, but I would expect there to be some kind of level of, 'Okay. Here are the resources that are pertinent.'" (Caregiver 11, vulvar cancer, stage unknown) "I would certainly want it updated. I would like to receive an initial with all updated information at the time of the appointment. If It's anything new developed in the meantime, any new significant treatments, anything based on study, yeah, that should be sent to people via mail, email, or both." (Caregiver 1, ovarian cancer, stage IV)

> *"I'm not too concerned with the physical stuff. I can deal with that. Her feet don't work. Her hands don't work. And she's had a profound hearing loss. I have no training background or anything in how to assist with that. But she'll say, "Can you open this for me?" … those easy things…. I'm more concerned with the emotional support and maybe being sensitive, those types of things." (Caregiver 7, Fallopian tube cancer, stage IIB).*

Fear of Recurrence. Fear of recurrence was common among both patients and caregivers (9/13 patients; 8/9 caregivers). Some patients reported overwhelming preoccupation with the chance that their cancer could return:

> *"I've had a lot of anxiety over it. Like if I get a pain, right away, my head goes to the worst-case scenario. So the fact that I had the cancer, it makes me more anxious about thinking that I could get it somewhere else." (Patient 3, fallopian tube cancer, stage IIB).*

Of interest, despite the majority confirming they experienced fear of recurrence, most also noted they were not preoccupied with this fear (10/13 patients; 2/9 caregivers).

Informational Needs. Informational needs were reported by both caregivers and patients and included possible signs or symptoms of recurrence (11/13 patients; 8/9 caregivers), management of side-effects (7/13 patients; 6/9 caregivers), contact information for care providers or sources of specialized services (6/13 patients; 2/9 caregivers), symptom management (4/13 patients, 4/9 caregivers) and methods to reduce risk of recurrence or new cancers (no patients; 5/9 caregivers).

Self-management and coping. Patients and caregivers wanted to know what the range of expected ongoing issues might be so that they could make informed decisions about when to contact their oncology HCP. Patients saw this as a way to self-manage and control their health:

> *"I am the best steward for my body. I'm the one that looks at it and feels it every day….I need to have as much education as I can have so that I can take care of my body" (Patient 8, ovarian cancer, stage IIIC).*

Caregivers felt similar desires:

> *"That would be my job to decide or not. But no, I don't want the medical providers deciding that. I want to know everything" (Caregiver 7, ovarian cancer, stage IIIB).*

Some patients did not want to be scared by the post-treatment side-effects:

> *"I don't like to get more information than what I really need to know. I don't want to scare myself.... I was going through this with just being calm and see what happens" (Patient 2, endometrial cancer, IA).*

Satisfaction with care. Although the majority reported satisfaction with the current informational resources they received from their oncology HCP (11/13 patients; 9/9 caregivers), almost all (12/13 patients; 9/9 caregivers) expressed a need for supplemental information to address their remaining issues and ongoing concerns. Most patients and caregivers reported feeling like they could contact their oncology HCP whenever they needed help:

> *"I'm not that concerned because I know that if something comes up and I'm unsure, I can call them and see them, or I can call them and ask them" (Patient 4, endometrial cancer, stage IIIA; and ovarian cancer, stage unknown).*

Survivorship care planning. Patients and caregivers mainly prefered to receive an SCP in written form (8/13 patients; 5/9 caregivers) though the majority noted that both written and online were acceptable (7/13 patients; 6/9 caregivers). Most wanted the SCP to be updated overtime (9/13 patients; 6/9 caregivers), and many wanted to receive the SCP at first follow-up visit (5/13 patients; 5/9 caregivers). Some did not think that a SCP would be applicable to them (3/13 patients; 1/9% caregivers) because they received minimal treatment:

> *"...They were very thorough with telling me everything that happened. Maybe it might have been different if I was getting further treatment like the chemo or radiation. I think you would want to know more information about that and how this is going to work or, I don't really know." (Patient 2, endometrial cancer, stage IA).*

While patients and caregivers varied in their preferences for the ideal content and timing of SCPs, most described their choices as based on their evolving state of health. Therefore, single review of treatment and care plan at the completion of initial therapy as a one time SCP to address survivorship concerns does not appear to be sufficient. Patients and caregivers wanted information when it would be immediately relevant to their health and well-being at multiple points across the disease trajectory:

> *"It all depends on my state of health. If I am very sick, I don't think I even need the information, but if I'm starting with symptoms, as soon as possible. So we, myself and my care team, will have that plan in motion for treatment." (Patient 1, ovarian cancer, stage IV).*

Ovarian versus non-ovarian cancer

Compared to patients with non-ovarian cancer types (n=7), patients with ovarian cancer (n=6) more often reported mood problems such as anxiety and depression (2/6 ovarian; 0/7 non-ovarian) and chemo-brain (2/6 ovarian; 0/7 non-ovarian), while non-ovarian cancer patients more often reported having no or limited symptoms (2/6 ovarian; 4/7 non-ovarian). Coping strategies of ovarian cancer patients were more often spiritual (4/6 ovarian; 1/7 non-ovarian) and trying to be optimistic (4/6 ovarian; 1/7 non-ovarian):

> *"I don't look back. Right now, I don't have cancer and I choose not to think that it's coming back. I'm very positive. I live for today and that's how I manage. I don't know about anybody else but that's my attitude." (Patient 1, ovarian cancer, stage IV).*

With regard to survivorship care planning, both ovarian cancer patients and caregivers preferred to receive written information (6/6 ovarian patients; 2/7non-ovarian patients; 4/5 ovarian caregivers; 1/4 non-ovarian caregivers). Many of the patients with other types of gynecological cancers – but none of the patients with ovarian cancer – reported that they were not interested in a SCP because it was not relevant to their situation (0/6 ovarian; 3/7 non-ovarian).

> *"I think this question [about SCPs] is more for people that have been through a lot more than what I have been through." (Patient 2, endometrial cancer, Stage IA).*

Perspectives of health care providers

The HCP focus group included a detailed discussion on the challenges they encounter while communicating about survivorship.. Illustrative quotations are presented below and additional quotes are stated in Table 3. A major barrier to communication was feeling an underlying tension between being direct about the likelihood of a recurrence without stripping away the patient's ability to enjoy life. They reported a reluctance to "scare" patients with information about recurrence and ongoing health issues as a way to help patients focus on enhancing their quality of life:

> *"There's always this really inherent tension in that visit, between stating that [the cancer is incurable] again, and taking away the reprieve that they're about to have.... The tension between being honest and being cruel, or being misleading. And it's very complex, and the language is very complex.... So it's a tight dance" (Provider 4, gynecologic oncologist).*

Table 3: Themes identified and exemplary quotes of health care providers

Theme	Description	Health care providers quotes
Challenges in post-treatment care	Challenges in communicating about survivorship, struggling to find necessary resources for patients, uncertainty about recurrence, not wanting to scare patients/ improve quality of life	"I think I use it as a sort of metric about my degree of burnout. If I'm looking at the end-game for them, and they're depressed about the potentially bad outcome, I feel like I'm a bit more burned-out. Whereas, if I'm celebrating with them now, I'm-- sort of feel like I understand the big picture, but where are they at now." (Provider 2, medical oncologist) "Helping people be able to use that good time that they have because I know that ovarian cancer patients actually spend a lot of that time just worrying and freaking out. And if care plan can help with that, but I'd be hopeful it might. Whereas for early stage in endometrial cancer patients, who we tell, "You're probably cured," I would actually want the care plan to be a little bit different and I actually want more there to be, like "If you have X kind of symptoms, or bleeding, or whatever, please give us a call." So I think, to me, I'd want them to be really shaped to what the general trajectory is that diseases tend to be." (Provider 7, gynecologic oncology fellow)
Need for survivorship care plan and resources	Need for SCP (most common issues/percentages, reassurance, sexual health, support groups, diet, exercise, attitude, how to get back to normal, what to expect, follow-up plan), written information as supplement to conversation, referencing what to look out for and when to come back, disease-specific SCPs	"I don't think I call it the survivorship plan. I think we just come up with a strategy for how they're going to move forward with or without their cancer. And we talk about what's sort of important." (Provider 1, gynecologic oncologist) "[Patients] seem to think that they're the only ones going through this process and they feel alone. And I never knew any of the resources to hook them up with. Like are there support groups out there? What are the resources they have so they don't feel so alone and can go forward in the survivorship period of their lives." (Provider 5, gynecologic oncology fellow) "if we had more of a standardized thing that we knew, oh, 80% of people have this, da, da, da, da, and you could kind of run through that check off and then have the immediate thing that they needed to get plugged into." (Provider 1, gynecologic oncologist)
Barriers to providing survivorship care plans	Barrier of time, not wanting to open up difficult needs, who should provide SCPs (oncologist, nurse, anybody), logistics of providing SCPs, standardized list of prompts / screening tools	"What if you ask somebody and they go to pieces in front of you, and then you have like a whole new thing and you don't have the ability to unpack it for an hour and a half. It's really hard. So how do you do that? And how do you make them feel like you've heard them?" (Provider 1, gynecologic oncologist)

Another challenge to communication was prognosis. For patients who were likely to experience a recurrence (e.g., patients with ovarian cancer), providers desired to reinforce that patients should live life in spite of fear and uncertainty:

> *"It's a question of how do we convey to patients that the time that they have in remission is precious and important? And they shouldn't delay life events thinking that they're going to have a really long time to sort of get to that later" (Provider 1, gynecologic oncologist).*

Despite the information available, HCPs felt they continued to struggle to find necessary resources for patients. They expressed the need for survivorship-care resources to facilitate and support conversations about what to expect after treatment including a follow-up plan. The examples described by one provider describe the extent and details of the resources providers wanted to provide their patients:

> *"I think it would be nice just to have resources about how to get back to your normal life. So what to do if you're depressed or anxious, or how to get sexual function back, or interest, or exercise. So, things not just about the cancer, but how can we get back to your life and living with the cancer" (Provider 6, gynecologic oncology fellow).*

Providers also expressed that they want tailored and disease-specific SCPs to assist with difficult conversations, particularly referring to ovarian cancer as being different from other gynecological cancers:

> *"Because you want to celebrate the win and not tell them that we're going to run out of runway" (Provider 1, gynecologic oncologist).*

However, the main barrier to providing a SCP to patients identified by providers was lack of time. In addition to concerns over time to develop and present a SCP, some worried that providing a SCP might identify needs or open up conversations that providers could not address during the visit. Gynecologic oncologists preferred to have a medical doctor or other member of the gynecological cancer team provide an SCP, but some felt that this could be provided by a dedicated survivorship specialist as opposed to no one providing SCPs.

DISCUSSION

This study reports participants' self-identified concerns and preferences for survivorship care. Findings indicate that patients with a gynecological cancer and their caregivers have needs and ongoing issues after treatment, such as side-effects and psychological distress, and that they desire information on how to better address these needs. Preferences for survivorship care largely differ across cancer types and individuals, with respect to content, timing, and mode of delivery and reflect the need for disease-specific, tailored SCPs and follow-up care to support care to the diverse group of gynecological cancer survivors. Our results contribute to the ongoing discussion about effective and efficient means to support survivorship care planning in gynecologic oncology, further highlighting the fact that 'one size fits all' approaches are unlikely to be successful, and individualized assessment and care planning is needed.

Issues, concerns and symptoms most often discussed in our study are similar to previous work and include pain, neuropathy, fatigue and mood problems such as anxiety, depression and fear of recurrence.[2-7] As reported in previous literature, ovarian cancer patients more often described mood problems and fear of recurrence or progression compared to non-ovarian cancer patients.[20] As a result, compared to non-ovarian cancer patients, ovarian cancer patients more often expressed a need for contact information or referral for someone to help with these concerns.

Caregivers in our study reported similar perspectives as patients, but with several notable exceptions including more frequent endorsement of being afraid of a cancer recurrence or disease progression and wanting to learn health promotion strategies. These results complement growing literature describing the changing and often increasing needs of caregivers of individuals with gynecological cancer.[21,22] For example, Stafford and Judd (2010) found that caregivers' unmet needs were a key predictor of their anxiety, depression, and relationship satisfaction.[23] Integrating caregivers' ongoing unmet needs such as those identified in our study into survivorship care can address their concerns and prevent these negative outcomes. Addressing the concerns and needs of caregivers as an aspect of survivorship care may reduce distress among patients and improve quality of life.

In spite of most patients and caregivers in our study being highly satisfied with information supplied by and resources identified by their HCPs, they still reported informational needs that remained unaddressed. Notably, some stakeholders wish to receive a written document including information about what to expect after treatment and extensive and up to date information on specific topics, which largely resembles a Survivorship Care Plan (SCP) as was proposed by the NAM since 2006.[11] However, other patients and

caregivers did not describe a clear need for additional resources or desire for more information. In this wide range of needs and preferences, a 'one size fits all' approach may not be most effective nor efficient. This might explain why previous trials assessing the effectiveness of SCPs failed to identify benefits in unselected populations, including samples of American.[13] and Dutch[16,17] gynecological cancer patients. Though women in the latter trial only included endometrial and ovarian cancer, previous analyses suggest that patients' benefit of SCPs is indeed heterogenous[24,25] Ideally, survivorship resources should be allocated to those with highest neccesity and be updated over time. This highlights a need for screening for informational and other needs as an important part of survivorship care, and a necessary step in the development of individualized SCPs. Future SCP effectiveness trials should focus on individualized SCPs, particularly when assessed in heterogenous patient populations such as in gynecological oncology.

As most patients and caregivers did not indicate a clear preference for either written or online SCPs, an online, patient-centered application including tailored information for those with specific needs could be a solution that fits the needs of all stakeholders. A written leaflet including more general information could complement the online tool, or even replace it for those with minimal information needs. Further, patients and caregivers who were interested in an SCP indicated that they would like to receive one during the first follow-up visit after the end of treatment, and prefer a conversation accompanied with it, as opposed to generation of a document alone. An important finding of this study is that patients and caregivers do not indicate a strong preference for the person leading this conversation. Conversely, HCPs in our study believe that patients prefer their treating oncologist to provide survivorship care planning. However, they also recognize that this may not be feasible in their practice due to increasing clinical burdens and lack of time. Previous studies also found that lack of time was cited as the greatest barrier to implementation of SCPs.[26,27] While oncologists buy into the concepts of survivorship care planning, the suggestions from providers in our study offer potential ways to address systematic implemention including personalization of care plans to individual patients, inclusion of a dedicated support staff to facilitate discussions, and creation of a prompt list to initiate the discussion using careful but clear communication strategies. Our study supports that patients and caregivers may be amenable to receive SCPs by other members of the care team besides the oncologist, depending on the clinical practices' logistics and feasibility.

This study includes a variety of gynecological cancer types and stages, caregiver types, and gynecologic oncology HCP. Even though our sample was reasonably heterogenous, we reached data saturation for all groups. Our qualitative data allowed for assessment of unique individual and hetergenous experiences of stakeholders. Our findings provide detailed in-depth descriptions of the various perspectives in this field and enrich the

limited literature available. However, a limitation of this study includes the use of a single medical center to recruit participants, serving patients with a relatively high socio-economic status and few ethnic minorities. Further, only one patient and her caregiver were clearly dissatisfied with care at our center, which is not in coherence with literature showing much higher proportions of dissatisfaction with care,[28,29] resulting in potentially biased descriptions of concerns and preferences.

Conclusion

In conclusion, patients and caregivers in this study endorsed the need for personalized, tailored survivorship care planning starting near the end of treatment. Patients with ovarian cancer reported qualitatively different experiences and desires as patient with non-ovarian gynecological cancers, indicating these groups may require distinct forms of care planning. HCPs require assistance in starting sensitive conversations at the end of treatment, but are open to providing individualized SCPs to their patients within the context of the entire team. These qualitative findings provide a description of the self-reported needs of multiple stakeholders, highlight barriers and opportunties to address survivorship needs within the gynecology oncology clinic, and can be used to support the development of patient-centered survivorship care planning interventions.

REFERENCES

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA: A cancer journal for clinicians.* 2015.
2. Donovan HS, Hartenbach EM, Method MW. Patient-provider communication and perceived control for women experiencing multiple symptoms associated with ovarian cancer. *Gynecologic oncology.* Nov 2005;99(2):404-411.
3. Ferrell B, Smith S, Cullinane C, Melancon C. Symptom concerns of women with ovarian cancer. *Journal of pain and symptom management.* Jun 2003;25(6):528-538.
4. Bradley S, Rose S, Lutgendorf S, Costanzo E, Anderson B. Quality of life and mental health in cervical and endometrial cancer survivors. *Gynecologic oncology.* 2006;100(3):479-486.
5. Greimel ER, Winter R, Kapp KS, Haas J. Quality of life and sexual functioning after cervical cancer treatment: A long-term follow-up study. *Psycho-Oncology.* 2009;18(5):476-482.
6. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *The International Journal of Psychiatry in Medicine.* 2010;40(2):163-181.
7. Abbott-Anderson K, Kwekkeboom KL. A systematic review of sexual concerns reported by gynecological cancer survivors. *Gynecologic oncology.* 2012;124(3):477-489.
8. Matulonis UA, Kornblith A, Lee H, et al. Long-term adjustment of early-stage ovarian cancer survivors. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society.* Nov-Dec 2008;18(6):1183-1193.
9. Mirabeau-Beale KL, Kornblith AB, Penson RT, et al. Comparison of the quality of life of early and advanced stage ovarian cancer survivors. *Gynecologic oncology.* Aug 2009;114(2):353-359.
10. Ozga M, Aghajanian C, Myers-Virtue S, et al. A systematic review of ovarian cancer and fear of recurrence. *Palliative & supportive care.* Dec 2015;13(6):1771-1780.
11. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
12. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. *Journal of Cancer Survivorship.* 2015;9(4):683-691.
13. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology.* 2013;129(3):554-558.
14. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology.* 2011;29(36):4755-4762.
15. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment.* 2013;138(3):795-806.
16. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology.* 2015;33(31):3550-3559.
17. de Rooij BH, Ezendam NPM, Nicolaije KAH, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecologic oncology.* May 2017;145(2):319-328.
18. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up – the ROGY Care trial. *Gynecologic Oncology (in press).* 2017.
19. Nekhlyudov L, Ganz PA, Arora NK, Rowland JH. Going Beyond Being Lost in Transition: A Decade of Progress in Cancer Survivorship. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jun 20 2017;35(18):1978-1981.
20. Ozga M, Aghajanian C, Myers-Virtue S, et al. A systematic review of ovarian cancer and fear of recurrence. *Palliative & supportive care.* 2015;13(6):1771-1780.
21. Petricone-Westwood D, Lebel S. Being a caregiver to patients with ovarian cancer: A scoping review of the literature. *Gynecologic oncology.* 2016;143(1):184-192.

22. Butow PN, Price MA, Bell ML, et al. Caring for women with ovarian cancer in the last year of life: A longitudinal study of caregiver quality of life, distress and unmet needs. *Gynecologic oncology.* 2014;132(3):690-697.
23. Stafford L, Judd F. Partners of long-term gynaecologic cancer survivors: psychiatric morbidity, psychosexual outcomes and supportive care needs. *Gynecologic oncology.* 2010;118(3):268-273.
24. de Rooij BH, Ezendam NP, Nicolaije KA, et al. Survivorship care plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients: the ROGY care trial. *Quality of Life Research.* 2018:1-12.
25. Nicolaije KA, Ezendam NP, Pijnenborg JM, et al. Paper-Based Survivorship Care Plans May be Less Helpful for Cancer Patients Who Search for Disease-Related Information on the Internet: Results of the Registrationsystem Oncological Gynecology (ROGY) Care Randomized Trial. *Journal of medical Internet research.* 2016;18(7).
26. Brennan M, Gormally J, Butow P, Boyle F, Spillane A. Survivorship care plans in cancer: a systematic review of care plan outcomes. *British journal of cancer.* 2014;111(10):1899-1908.
27. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
28. Nicolaije KA, Husson O, Ezendam NP, et al. Endometrial cancer survivors are unsatisfied with received information about diagnosis, treatment and follow-up: a study from the population-based PROFILES registry. *Patient education and counseling.* Sep 2012;88(3):427-435.
29. Jones JM, Ferguson S, Edwards E, Walton T, McCurdy N, Howell D. Experiences of care delivery: endometrial cancer survivors at end of treatment. *Gynecologic oncology.* 2012;124(3):458-464.

Chapter 9

Recurrent cancer is associated with dissatisfaction with care - a longitudinal analysis among ovarian and endometrial cancer patients

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ABSTRACT

Objective: The primary aim of this study was to assess the longitudinal impact of a recurrence of gynecological cancer on satisfaction with information provision and care. The secondary aim was to assess the impact of a recurrence on illness perceptions, anxiety and depression and health-related quality of life (HRQoL).

Methods/ materials: This study is a longitudinal analysis from the ROGY Care trial, conducted between 2011 and 2014, including patients with endometrial (N=215) and ovarian (N=149) cancer. Patients were invited to complete questionnaires directly after initial treatment and after 6, 12 and 24 months. Satisfaction with information provision and care, illness perceptions, anxiety and depression were compared before and after the recurrence. Linear mixed model analyses were conducted to assess the differences in outcomes of patients with a recurrence compared to patients without a recurrence.

Results: During 2-year follow-up, 25 patients with endometrial cancer (12%) and 64 patients with ovarian cancer (43%) had recurrent disease, of whom 9 endometrial and 26 ovarian cancer patients completed at least one questionnaire after their recurrence was determined. Patients reported lower satisfaction with care after the diagnosis of a recurrence (doctor interpersonal skills, exchange of information between caregivers and general satisfaction with care) compared to patients without recurrence. In addition, patients reported lower HRQoL, more anxiety and depression more threatening illness perceptions after diagnosis of a recurrence.

Conclusion: After diagnosis of recurrent disease, endometrial and ovarian cancer patients were less satisfied with care compared to patients without a recurrence. Our findings suggest that patients with recurrent cancer are in need of care that is better tailored to their needs.

INTRODUCTION

Over the past decades, the number of cancer survivors has rapidly increased, due to earlier diagnosis, improved treatment options and ageing. In 2016, there were about 15.5 million cancer survivors in the United States, and this number is expected to increase to 20.3 million in 2026.[1] This increasing cohort of cancer survivors remains at risk for long-term physical and psychosocial effects. Therefore, alongside crude survival, patient-reported outcomes (PROs) are increasingly acknowledged to be important aspects of treatment efficacy.[2-5]

One of the main concerns of cancer patients is the possibility of recurrent disease followed by palliative treatment and imminent death.[6] In gynecological cancer, the risk of recurrence is highest in ovarian cancer due to its usual diagnosis at an advanced stage of the disease; 75% of all ovarian cancer patients will eventually get recurrent disease.[7] In contrast, endometrial cancer usually presents at an early stage and therefore generally has a good prognosis.[8] However, even in low-stage endometrial cancer about 6% of the patients will have recurrent disease.[8,9] Regardless of the risk of recurrence, fear of cancer recurrence seems to be a universal concern of cancer survivors.[6,10] Thus, insecurity about new and remaining symptoms after cancer treatment and the possibility that these symptoms may indicate the presence of a recurrence may negatively affect quality of life and increase health care use.[11,12]

Previous research shows that psychological responses to cancer recurrence include the loss of hope for recovery, anxiety and depressive symptoms, fear of death and difficulties with disability.[10,13-16] In breast cancer survivors, patients with recurrent cancer experience lower anxiety and confusion compared to patients after their first diagnosis of cancer, but worse health-related quality of life (HRQoL), poorer physical functioning, and higher cancer related distress compared to patients without a recurrence.[17,18] Similarly, a recent study in patients with recurrent ovarian cancer showed high levels of anxiety and depression among these patients, but anxiety decreased during active treatment of the recurrence .[19]

Little is known about satisfaction with information provision and care in patients with a recurrence. Qualitative studies suggest that patients with a recurrence are less satisfied with communication with their health care providers compared to before the recurrence, because they felt no longer heard about their concerns and symptom.[20,21] A study in patients with recurrent digestive cancer requiring palliative care shows that low satisfaction with care is associated with low HRQoL[22]. To our knowledge, no quantitative studies have addressed the impact of a cancer recurrence on satisfaction with information provision and care.

Therefore, the main aim of the current study is to assess the longitudinal impact of a recurrence on satisfaction with information provision and care in endometrial and ovarian cancer patients. Secondary, we aim to assess the impact of a recurrence on illness perceptions, anxiety and depression and health-related quality of life. We hypothesize that patients who develop a recurrence are disappointed with their outcome and therefore experience lower satisfaction with information provision and care compared to before their recurrence was determined as well as compared to patients without a recurrence.

METHODS

Design

This study included endometrial and ovarian cancer patients from the ROGY Care trial. Details of the ROGY Care trial are described in the protocol paper.[23] The effects of Survivorship Care Plans (SCPs) on health care provider and patient-reported outcomes have been described previously.[24,25] The present study uses the trial data as an observational prospective dataset and does not assess the effects of SCPs.

Participants and recruitment

All patients with newly diagnosed endometrial cancer (N=221) between April 2011 and October 2012 or ovarian cancer (N=174) between April 2011 and March 2014 were invited to participate to the ROGY Care trial with a letter and informed consent by their treating gynecologist. Follow-up questionnaires were sent to the patients after initial treatment, at 6, 12 and 24 months after treatment. Patients with primary progressive disease (endometrial cancer N=6 and ovarian cancer N=25) were excluded from the current analysis (Figure 1).

Measures

Questionnaires included all primary and secondary outcome measures at each time-point. Outcomes were assessed with validated measures shown to have acceptable psychometric properties. Additional clinical data were obtained from the Netherlands Cancer Registry (NCR), including date of diagnosis, cancer type, FIGO (Federation International of Gynecology and Obstetrics) stage and primary treatment. After closing of the trial in July 2016, additional information on the presence or absence of recurrence, date of recurrence and the provided treatment for recurrence were extracted from the medical records retrospectively.

Primary outcome measures

Satisfaction with information provision was assessed with the EORTC (European Organization for Research and Treatment of Cancer) INFO25.[26] Scales included four multi-item subscales (information about the disease, medical tests, treatment and other care

services) and four single-item scales (information about different places of care, things you can do to help yourself get well, satisfaction with the information, helpfulness of the information). All scales were converted to a score between 0 (low perceived information provision) and 100 (high perceived information provision). Additional remarks about satisfaction with information provision were examined to find explanations for our findings.

Satisfaction with care was assessed with the EORTC INPATSAT32.[27] Scales included three multi-item scales (doctor's interpersonal skills, doctor's technical skills and doctor's information provision) and two singe-items scales (exchange of information between caregivers and general satisfaction with care). All scales were converted to a score between 0 (low perceived quality of care) and 100 (high perceived quality of care).

Secondary outcome measures

Illness perception was assessed with the Brief Illness Perception Questionnaire (B-IPQ).[28] Scales included eight single-items regarding cognitive illness representations (how much illness affects life, how long illness will continue, how much patient has control over illness, how much treatment helps to cure illness, how many symptoms are experienced), emotional representations (how concerned patient is about illness, how much patient is affected emotionally) and comprehensiveness (how well patient understands illness). Patients indicated their endorsement with an item on a scale between 1 (low endorsement) and 10 (high endorsement).

Anxiety and depression was assessed with the Hospital Anxiety and Depression scale (HADS).[29] Scales included 7 items for anxiety and 7 items for depression. Each item indicated a score between 0 (no anxiety or depression) and 3 (the worst anxiety or depression). The sum of these items resulted in two subscales for anxiety and depression, ranging between 0 and 21.

HRQoL was assessed with the EORTC QLQ-C30.[30] This questionnaire included multiple scales: global QoL, function scales (physical, role, emotional, cognitive, social) and symptom scales (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties). All scales were converted to a score between 0 (low QoL/no symptoms) and 100 (high QoL/a lot of symptoms).

Statistical Analysis

The data were analyzed using Statistical Analysis System (SAS) version 9.4 (SAS Institute, Cary, NC, 1999). Differences were considered statistically significant at a p-value ≤ 0.05. Differences in patients and tumor characteristics between patients with and without recurrent disease were analyzed using the t-tests for normally distributed continuous variables and chi-square tests for categorical variables.

Longitudinal changes in outcomes before and after recurrence were analyzed using dependent samples t-tests. In this analysis, only patients with a recurrence who completed at least one questionnaire before and after recurrence were included (N=35). Measurement time-points included in the analyses differ by time of recurrence (either 0 and 6, 6 and 12, or 12 and 24 months after initial treatment). Patients without a recurrence during follow-up were randomly matched to patients with a recurrence on tumor type and questionnaire time-points (N=35), resulting in a representative control group with equal numbers of endometrial and ovarian cancer patients, and equal time-point distribution likewise the patients with a recurrence. Visual representations of longitudinal changes in PROs were computed for patients with a recurrence on the available data of time-points before and the available time-points after recurrence and the matched patients without a recurrence.

Multilevel linear mixed models were used to assess the between-subject effects of having a recurrence on outcomes, allowing for adjustment of inter-dependency between repeated measures within patients[31], and correction for missing data at random.[32] In this analysis, all patients with (N=35) and without (N=255) a recurrence, and all time-points (after initial treatment, after 6, 12, and 24 months) were included. Overall effects were assessed comparing outcomes of observations of patients with a recurrence (after diagnosis of recurrent disease) to all observations of patients without a recurrence (including patients before diagnosis of recurrent disease). In the crude model, no adjustments were made for time-point or cancer type and therefore the crude means may show biased results. In the adjusted model, adjustments were made for all a-priori selected covariates, including time-point (after diagnosis, after 6, 12, and 24 months), age, socio-economic status, cancer type, FIGO stage, primary treatment (chemotherapy, radiotherapy), employment status, marital status, and trial allocation (SCP care versus usual care).

RESULTS

Of the 544 patients who received an invitation to participate in the trial, 395 patients (73%) completed the first questionnaire, of which 221 patients had endometrial cancer (75%) and 174 patients had ovarian cancer (70%). Questionnaires were completed by 282 patients (52%) after 6 months, 248 patients (46%) after 12 months, and 203 patients (37%) after 24 months. Over 24 months, 25 patients with endometrial cancer (12%) and 64 patients with ovarian cancer (43%) had recurrent disease (Figure 1). Only 35 patients with a recurrence completed at least one questionnaire after recurrence, of whom 9 patients with endometrial cancer and 26 patients with ovarian cancer.

No statistical tests were conducted to assess the differences in baseline characteristics between patients with and without a recurrence because numbers of patients with a recurrence were too small. However, higher tumor stages are observed in patients with a recurrence (FIGO stage III and IV, 33% vs. 3% in endometrial; 80% vs. 29% in ovarian; Table 1).

Outcomes were significantly different after diagnosis of a recurrence, compared to before recurrence: patients reported lower satisfaction with information about the treatment (P<0.03), other services (P<0.03), doctor technical skills (P=0.04), doctor interpersonal skills (P=0.01), doctor information provision (P=0.03), exchange of information between caregivers (P=0.01) and lower general satisfaction with care (P<0.01) after diagnosis of a recurrence compared to before. No differences in outcomes were found between patients with and without a recurrence at the matched-time points (Table 2; Figure 2).

In addition, patients with a recurrence reported also a significantly more threatening illness perceptions; more anxiety and depressive symptoms; lower global QoL and more physical symptoms after a recurrence then before the recurrence. (Appendix 1).
In multilevel linear analysis, patients with a recurrence compared to patients without a recurrence reported significantly lower satisfaction with doctor interpersonal skills (β=-7.7, P<0.01), exchange of information between caregivers (β=-7.5, P<.0.01) and general satisfaction with care (β=-7.9, P<0.01), after adjustment for potential covariates.

In the remarks patients with a recurrence made in the open fields of the questionnaire, a variation was observed in the perceived of amount of information received from care providers. Some wanted to have had more information on recurrence ('Generally doctors give less information about the cancer.'), and others did not want too much information ('I don't want too much information, it makes me ill.').

DISCUSSION

In endometrial and ovarian cancer patients with a recurrence, we found lower satisfaction with care after their recurrence was determined, compared to before a recurrence and compared to patients without a recurrence. No differences were found in satisfaction with information provision between patients with and without a recurrence.

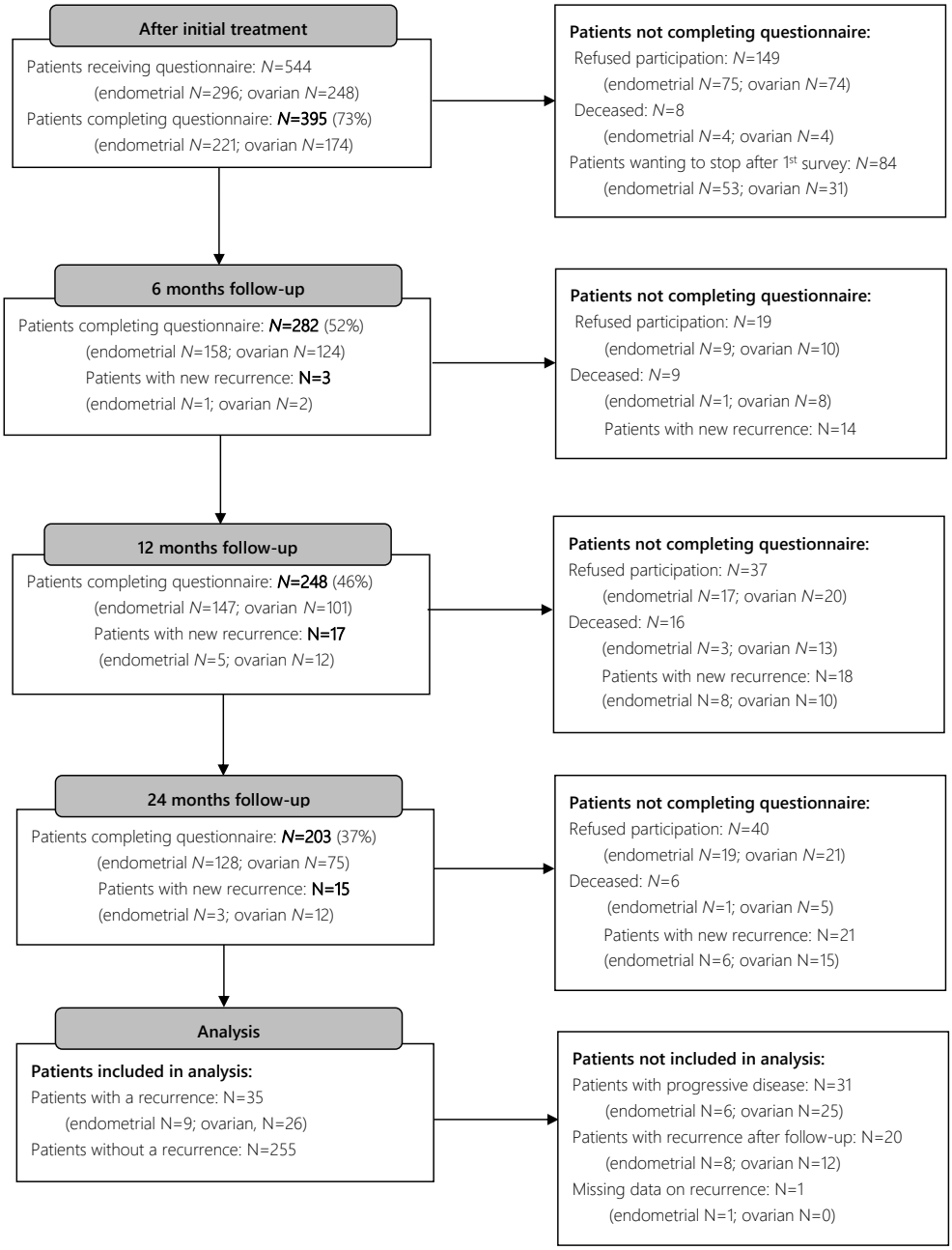


Figure 1: Flow diagram of patient enrolment and follow-up of endometrial and ovarian cancer patients

Table 1: Baseline characteristics of endometrial and ovarian cancer survivors, with and without recurrence during follow-up

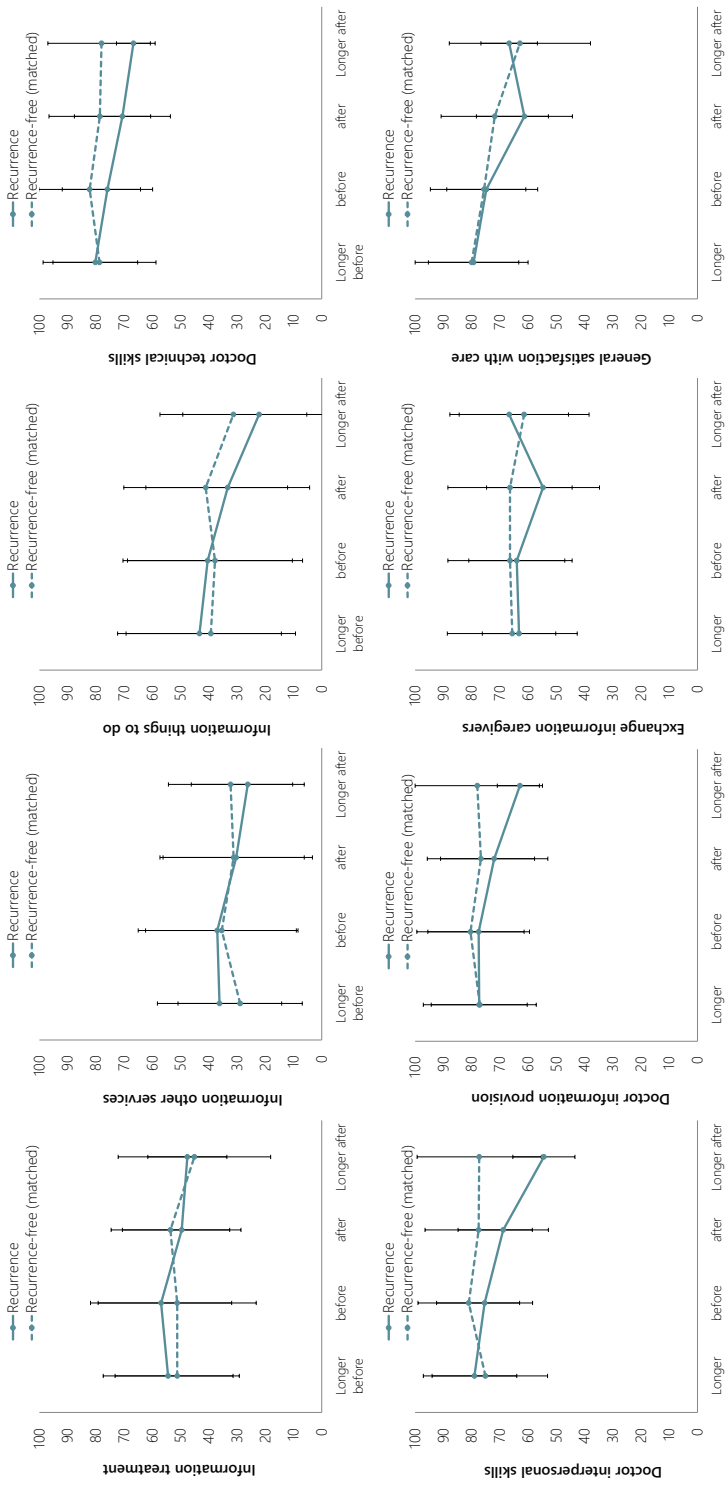
	ENDOMETRIAL CANCER		OVARIAN CANCER	
	Recurrence N=9	Recurrence-free N=182	Recurrence N=26	Recurrence-free N=73
Age at survey, mean (SD)	68.2 (5)	67.5 (9)	64.9 (9)	59.6 (12)
SES, n (%)				
High	5 (56)	65 (38)	10 (48)	26 (38)
Intermediate	2 (22)	76 (43)	7 (33)	29 (43)
Low	2 (22)	34 (19)	4 (19)	13 (19)
Comorbidity, n (%)				
None	1 (11)	33 (19)	6 (23)	23 (32)
1	0 (0)	48 (27)	8 (31)	20 (28)
2 or more	8 (89)	97 (55)	12 (46)	29 (40)
Marital status[1], n (%)				
Partner	7 (78)	135 (75)	19 (73)	57 (78)
No partner	2 (22)	44 (25)	7 (27)	16 (22)
Employed, n (%)				
Yes	0 (0)	35 (21)	10 (38)	28 (38)
No	8 (100)	133 (79)	16 (62)	45 (61)
FIGO-stage, n (%)				
I	6 (67)	174 (96)	3 (12)	43 (60)
II	0 (0)	4 (2)	2 (8)	8 (11)
III	2 (22)	3 (2)	17 (68)	16 (22)
IV	1 (11)	1 (1)	3 (12)	5 (7)
Primary treatment, n (%)				
Chemotherapy	2 (22)	2 (1)	26 (100)	39 (54)
Radiotherapy	6 (67)	56 (31)	0 (0)	0 (0)
Recurrence characteristics				
Months to recurrence				
Mean (SD)	15.0 (4.6)		15.8 (5.4)	
Treatment recurrence, n (%)				
Chemotherapy	5 (56)		17 (81)	
Radiotherapy	1 (11)		1 (5)	
Hormonal therapy	2 (22)		1 (5)	

Note: patients were excluded when having a primary progressive cancer (endometrial, N=6; ovarian, N=25), or when they did not complete any survey after recurrence (endometrial, N=23 ; ovarian, N=50).

Table 2: Primary outcome measures of patient-reported outcomes in patients with recurrence and matched patients without recurrence, dependent samples t-tests

	Patients with recurrence[a]				Matched patients without recurrence[b]		
	N	Before recurrence, M (SD)	After recurrence, M (SD)	Mean change	Matched time-point before, M (SD)	Matched time-point after, M (SD)	Mean change
Satisfaction with information provision (INFO-25)							
Information disease	34	57.8 (24)	57.4 (25)	-0.4	61.3 (19)	60.5 (23)	-0.8
Information medical tests	34	69.0 (31)	65.7 (27)	-3.3	71.0 (21)	72.4 (22)	1.4
Information treatment	33	56.9 (25)	49.6 (21)	**-7.3***	51.2 (28)	51.9 (26)	0.7
Information other services	35	37.0 (28)	30.3 (27)	**-6.7***	35.4 (27)	31.2 (24)	-4.2
Information places to go	34	34.3 (34)	29.4 (34)	-4.9	27.6 (31)	26.4 (34)	-1.2
Information things to do	33	40.4 (30)	33.3 (29)	-7.1	37.8 (31)	41.1 (29)	3.3
Satisfaction Information	33	69.7 (24)	65.7 (23)	-4.0	76.0 (19)	68.8 (22)	-7.3
Helpfulness information	30	73.3 (20)	67.8 (22)	-5.4	75.3 (23)	72.0 (23)	-3.7
Satisfaction with care (INPATSAT-32)							
Doctor technical skills	34	75.9 (16)	70.6 (17)	**-5.3***	82.2 (19)	78.6 (18)	-3.6
Doctor interpersonal skills	32	75.4 (17)	68.8 (16)	**-6.6***	81.0 (18)	77.5 (19)	-3.5
Doctor information provision	34	77.5 (18)	72.0 (19)	**-5.5***	80.4 (19)	76.7 (19)	-3.7
Exchange information caregivers	30	64.0 (17)	54.7 (20)	**-9.3***	66.4 (22)	66.4 (22)	0.0
General satisfaction with care	31	74.8 (14)	61.3 (17)	**-13.5****	75.6 (19)	71.9 (19)	-3.7

[a]Measurement time-points differ by time of recurrence between time-points, either 0 and 6, 6 and 12, or 12 and 24 months after initial treatment. [b]patients without recurrence were randomly matched to patients with recurrence on tumor type and time-points of questionnaire (i.e. the ratios of tumor type and measured time-points are equal in recurrence versus non-recurrence groups). Dependent samples t-tests were performed. *P<0.05, **P<0.01.



Note: Measurement time-points differ by time of recurrence between time-points. Time-points longer before indicate patient reported outcomes two questionnaires before recurrence (N=30) or matched time-point in patients without a recurrence (N=30), time-points longer after indicate patient reported outcomes two questionnaires after recurrence (N=8) or matched time-point in patients without a recurrence (N=17). Time-points before and after recurrence or matched time-points for all outcome variables are shown in table 2 (N=35).

Figure 2: longitudinal patient-reported outcomes in patients who develop a recurrence versus matched patients without a recurrence

Table 3: multilevel linear mixed model analysis, overall between-subjects effects of recurrence versus no recurrence (all time-points: after diagnosis, after 6, 12, and 24 months)

	N obs in analysis	No recurrence, crude M (SE)	Recurrence, crude M (SE)	Crude β (95% CI)	Adjusted β (95% CI)a
Satisfaction with information provision (INFO-25)					
Information disease	1034	60.7 (1.0)	59.4 (2.7)	-1.3 (-6.6; 4.0)	1.3 (-4.2; 6.7)
Information medical tests	1025	69.2 (1.1)	64.7 (2.8)	-4.5 (-10.0; 1.1)	-1.6 (-7.4; 4.2)
Information treatment	1021	50.8 (1.1)	45.8 (3.4)	-5.0 (-11.6; 1.6)	-5.8 (-12.4; 0.8)
Information other services	1033	30.9 (1.2)	26.7 (3.2)	-4.2 (-10.5; 2.2)	-5.5 (-11.8; 0.7)
Information places to go	979	25.6 (1.3)	22.5 (4.5)	-3.1 (-11.9; 5.7)	-5.1 (-14.4; 4.1)
Information things to do	940	40.9 (1.4)	32.1 (4.9)	-8.8 (-17.7; 0.2)	-5.3 (-15.2; 4.6)
Satisfaction Information	1019	72.3 (1.1)	65.2 (3.4)	**-7.7 (-13.4; -0.8)***	-2.7 (-9.1; 3.8)
Helpfulness information	990	72.2 (1.1)	67.6 (3.6)	-4.6 (-11.2; 2.0)	0.4 (-6.4; 7.2)
Satisfaction with care (INPATSAT-32)					
Doctor technical skills	999	79.4 (0.8)	72.1 (2.2)	**-7.3 (-11.6; -3.0)****	-4.4 (-8.9; 0.2)
Doctor interpersonal skills	1013	76.5 (0.9)	67.0 (2.3)	**-9.5 (-14.0; -5.0)****	**-7.7 (-12.4; -2.9)****
Doctor information provision	1029	77.7 (0.9)	71.4 (2.2)	**-6.3 (-10.6; -2.0)****	-4.0 (-8.5; 0.5)
Exchange information caregivers	998	66.8 (0.9)	58.2 (2.7)	**-8.6 (-13.8; -3.4)***	**-7.5 (-13.1; -1.9)****
General satisfaction with care	1013	75.8 (0.8)	61.5 (2.8)	**-14.3 (-19.8; -8.8)****	**-7.9 (-13.3; -2.4)****

Note: patients were excluded when having a primary progressive cancer (endometrial, N=6; ovarian, N=25).
[a]Analysis was adjusted for time-point (after diagnosis, after 6, 12, and 24 months), age, socio-economic status, cancer type, FIGO stage, primary treatment (chemotherapy, radiotherapy), employment status, marital status, and trial allocation (SCP care versus usual care). *P<0.05, **P<0.01.

Patients with a recurrence reported significantly lower satisfaction with the interpersonal skills of the doctor, exchange of information between caregivers and general satisfaction with care compared to patients without a recurrence. Possibly, decreased satisfaction with care after diagnosis of a recurrence could be explained by an overall feeling of dissatisfaction due to the poor prognosis and more treatments. More effort may be needed to improve information exchange between hospitals ('The communication between the hospital where I have had surgery and the hospital where I had my follow up was very bad. How could it be, that I had to bring the results of the surgery to my doctor by myself?'). A trial in patients with recurrent ovarian cancer shows that internet-based interventions for symptom management could improve patient-clinician communication and increase quality of life.

Early conversations about goals and planning of care and increased access to early palliative care services may be needed to provide necessary support for patients with recurrent cancer. A trial in recurrent ovarian cancer demonstrated that early palliative care is cost-

effective and cost saving, but effects on patient reported outcomes are understudied.[33] Another trial shows that rehabilitation in a hospice day care unit reduced the unmet needs for psychological support for patients with advanced, recurrent or progressive cancer. [34] Future intervention studies are needed to investigate the most optimal means to improve care for patients with recurrent cancer and to overcome barriers to integration of palliative care. [35,36].

In contrast to earlier studies and to our hypothesis, our study indicated that having a recurrence does not change overall satisfaction with information provision. A study about experiences of patients with recurrent ovarian cancer described that patients with a recurrence felt a change in the attitude of healthcare professionals and they felt that communication became strained between themselves and health professionals.[20] Patients with a recurrence felt that information about treatment options was more difficult to obtain after the recurrence was determined than at the time of their initial diagnosis and interpreted this change as loss of hope of the care provider.[20] However, another qualitative study suggests that health care providers aim to tailor their information provision to their perception of patients' needs. [37]

Our findings on the impact of recurrence on HRQoL and anxiety and depression are similar to previous studies in patients with a recurrence[20,38], which also found that patients with recurrent cancer have a lower HRQoL and more anxiety. We found that physical functioning, role functioning and social functioning were significantly decreased, while fatigue, nausea and vomiting, insomnia anxiety and depression were increased in patients with a recurrence. While not all of these domains can be improved by treatment, accurate detection of these problems and adequate referral to for example psychosocial care is important during follow-up.

An important strength of the current study is our representative sample of endometrial and ovarian cancer patients due to the population-based sampling and high response rates (73%). The longitudinal design with 2-year follow-up gave the opportunity to compare outcome measures before and after recurrent cancer. Due to these strengths, the results of this study reflect daily clinical practice. Another strength of this study was the possibility to adjust for both socio-demographic and clinical confounders due to the complete and thorough data collection.

A limitation that should be noted is the low number of patients with a recurrence. Only a limited number of patients completed a questionnaire after the recurrence was determined, resulting in a selective sample of those with lower cancer stages. Due to these small numbers, we could not assess the impact of survivorship care plans in patients with a recurrence, nor could we stratify the results for endometrial and ovarian cancer.

However, our findings were similar in both cancer types. Another limitation is that in the longitudinal analyses of patients with and without recurrence separately, we could not match for stage, while stage may explain some of our findings. However, in multilevel linear mixed models we adjusted for stage as a covariate and results remained similar. Future research should study larger groups of patients with recurrent cancer, and different cancer types to make results more generalizable.

Our findings suggest that follow-up care needs to be tailored to the needs of patients after diagnosis of a recurrence, since their needs seem to be different from those without a recurrence. More effort may be needed to better communicate the goals and possibilities of care and to provide early palliative care in case of cancer recurrence, as a means to support patients in the onset of coping with a fatal prognosis. Possibly, for some patients with a recurrence, follow-up care should not only be directed at medical- but also at non-medical issues. Other patients with a recurrence may prefer less information, less visits and CT scans. Further research is needed to identify what type of patients have what type of needs after diagnosis of a recurrence. Our guidelines should provide more room for individual patient's needs and a tailor-made approach. By shared decision making, a more tailored treatment and follow-up plan could be designed for patients with recurrent disease.

In conclusion, endometrial and ovarian cancer patients are less satisfied with care after diagnosis of recurrent disease. Our results suggest that more attention should be paid to the care for patients with a recurrence as their care needs seem to be different from patients without a recurrence in routine follow-up care.

APPENDIX 1

Secondary outcome measures of patient-reported outcomes in patients with recurrence and matched patients without recurrence, dependent samples t-tests

	Patients with recurrence[a]				Matched patients without recurrence[b]		
	N	Before recurrence, M (SD)	After recurrence, M (SD)	Mean change	Matched time-point before, M (SD)	Matched time-point after, M (SD)	Mean change
Illness perceptions (BIPQ)							
How much illness affects life	33	5.4 (2.8)	6.8 (2.4)	**1.4****	4.5 (2.9)	4.2 (2.6)	-0.3
How long illness will continue	30	5.4 (3.3)	9.3 (1.6)	**3.9****	4.4 (3.0)	4.8 (3.4)	0.4
How much control over illness	31	4.5 (3.0)	3.4 (2.7)	-1.1	5.4 (3.0)	5.0 (3.2)	-0.4
How much treatment helps to cure	32	6.9 (2.4)	5.8 (2.7)	-1.1	6.7 (3.0)	7.0 (2.8)	0.2
How much symptoms experienced	32	4.7 (2.3)	5.7 (2.6)	1	3.9 (2.6)	3.6 (2.6)	-0.3
How concerned about illness	33	5.7 (3.2)	7.5 (2.4)	**1.8****	4.4 (2.7)	4.7 (2.6)	0.3
How well understand illness	33	7.6 (2.5)	6.7 (3.4)	-0.9	6.2 (2.8)	6.1 (3.1)	-0.4
How much affects emotionally	33	5.0 (2.9)	6.2 (2.7)	**1.2***	4.2 (2.6)	4.2 (2.6)	0.0
Anxiety and depression (HADS)							
Anxiety symptoms	33	5.5 (4.0)	7.6 (4.7)	**2.1****	4.8 (4.5)	4.5 (3.4)	-0.3
Depressive symptoms	28	3.5 (3.3)	6.0 (3.9)	**2.5****	3.4 (3.3)	2.9 (2.9)	-0.5
Health-related quality of life (EORTC QLQ-C30)							
Global quality of life	35	75.7 (16)	61.7 (25)	**-14.0****	79.8 (18)	82.9 (14)	3.1
Function scales							
Physical Functioning	33	77.7 (20)	69.7 (20)	**-8.0***	83.9 (20)	83.6 (18)	-0.3
Role Functioning	33	73.2 (29)	62.6 (30)	-10.6	78.1 (31)	81.4 (25)	3.3
Emotional functioning	35	80.9 (21)	75.5 (22)	-5.4	81.0 (24)	82.9 (17)	-1.9
Cognitive functioning	35	81.4 (17)	80.5 (17)	-0.9	81.0 (25)	88.1 (17)	**7.1***
Social functioning	35	82.9 (21)	76.7 (23)	-6.2	85.7 (22)	86.7 (19)	1.0
Symptom scales							
Fatigue	35	31.9 (24)	41.3 (26)	**9.4***	25.4 (22)	21.3 (25)	-4.1
Nausea and vomiting	35	7.1 (12)	13.8 (20)	6.7	1.9 (5)	3.3 (10)	1.4

	Patients with recurrence[a]				Matched patients without recurrence[b]		
	N	Before recurrence, M (SD)	After recurrence, M (SD)	Mean change	Matched time-point before, M (SD)	Matched time-point after, M (SD)	Mean change
Pain	35	17.1 (21)	25.7 (25)	**8.6***	15.7 (22)	18.1 (25)	2.4
Dyspnea	35	19.0 (25)	16.2 (20)	-2.8	15.2 (23)	8.6 (22)	6.7
Insomnia	35	29.5 (25)	37.1 (33)	8.6	34.3 (36)	25.7 (32)	-8.6
Appetite loss	34	11.4 (20)	21.9 (29)	10.5	5.7 (17)	1.9 (11)	-3.8
Constipation	34	18.1 (26)	18.1 (25)	0.0	6.6 (22)	7.6 (20)	-1.0
Diarrhea	34	9.8 (21)	13.7 (25)	3.9	7.6 (22)	3.8 (18)	-3.8
Financial difficulties	30	2.9 (10)	8.6 (20)	**5.6***	6.7 (19)	7.6 (26)	0.9

[a]Measurement time-points differ by time of recurrence between time-points, either 0 and 6, 6 and 12, or 12 and 24 months after initial treatment. [b]patients without recurrence were randomly matched to patients with recurrence on tumor type and time-points of questionnaire (i.e. the ratios of tumor type and measured time-points are equal in recurrence versus non-recurrence groups). Dependent samples t-tests were performed. *P<0.05, **P<0.01.

REFERENCES

1. Miller K, Siegel R, Lin C, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016;66(4):271-289.
2. Ayanian J, Jacobsen P. Enhancing research on cancer survivors. *J Clin Oncol.* 2006;24:5149-5153.
3. Mallinger J, Griggs J, Shields C. Patient-centered care and breast cancer survivors' satisfaction with information. *Patient Educ Couns.* 2005;57:342-349.
4. Rutten L, Arora N, Bakos A, et al. . Information needs and sources of information among cancer patients: a systematic review of research (1980–2003). *Patient Educ Couns.* 2005;57(3):251-261.
5. Husson O, Mols F, van de Poll-Franse L. The relation between information provision and health related quality of life, anxiety and depression among cancer survivors: a systematic review. *Ann Oncol* 2011;22:761-772.
6. van de Wal M, van de Poll-Franse L, Prins J, Gielissen M. Does fear of cancer recurrence differ between cancer types? A study from the population-based PROFILES registry. *Psychooncology.* 2016;25(7):772-778.
7. Eng K, Hanlon B, Bradley W, Szender J. Prognostic factors modifying the treatment-free interval in recurrent ovarian cancer. *Gynecol Oncol.* 2015;139(2):228-235.
8. Amant F, Mirza M, Koskas M, Creutzberg C. Cancer of the corpus uteri. *Int J Gynaecol Obstet.* 2015;131:Suppl 2:S96-104.
9. Jeppesen M, Mogensen O, Hansen D, Iachina M, Korsholm M, Jensen P. Detection of recurrence in early stage endometrial cancer - the role of symptoms and routine follow-up. *Acta Oncol.* 2017;56(2):262-269.
10. Hanprasertpong J, Geater A, Jiamset I, Padungkul L, Hirunkajonpan P, Songhong N. Fear of cancer recurrence and its predictors among cervical cancer survivors. *Journal of gynecologic oncology.* 2017;28(6).
11. Simard S, Thewes B, Humphris G, et al. Fear of cancer recurrence in adult cancer survivors: a systematic review of quantitative studies. *J Cancer Surviv.* 2013;7(3):300-322.
12. Koch L, Jansen L, Brenner H, Arndt V. Fear of recurrence and disease progression in long-term (≥ 5 years) cancer survivors--a systematic review of quantitative studies. *Psychooncology.* 2013;22(1):1-11.
13. Mahon S, Cella D, Donovan M. Psychosocial adjustment to recurrent cancer. *Oncol Nurs Forum.* 1990;17(Suppl.):47-52.
14. Mahon S, Casperson D. Exploring the psychosocial meaning of recurrent cancer: a descriptive study. *Cancer Nurs.* 1997;20:178-186.
15. Munkres A, Oberst M, Hughes S. Appraisal of illness, symptom distress, self-care burden, and mood states in patients receiving chemotherapy for initial and recurrent cancer. *Oncol Nurs Forum.* 1992;19:1201-1209.
16. Weisman A, Worden J. The emotional impact of recurrent cancer. *J Psychosocial Oncol.* 1985;3:5-16.
17. Andersen B, Shapiro C, Farrar W, Crespin T, Wells-Digregorio S. Psychological responses to cancer recurrence. *Cancer.* 2005;104(7):1540-1547.
18. Yang H, Thornton L, Shapiro C, Andersen B. Surviving recurrence: psychological and quality-of-life recovery. *Cancer.* 2008;112(5):1178-1187.
19. Wen Q, Shao Z, Zhang P, Zhu T, Li D, Wang S. Mental distress, quality of life and social support in recurrent ovarian cancer patients during active chemotherapy. *European Journal of Obstetrics & Gynecology and Reproductive Biology.* 2017;216:85-91.
20. Howell D, Fitch M, Deane K. Women's experiences with recurrent ovarian cancer. *Cancer Nurs.* 2003;26(1):10-17.
21. Mahon S, Cella D, Donovan M. Psychosocial adjustment to recurrent cancer. Paper presented at: Oncology nursing forum1990.
22. Morishita M, Kamibeppu K. Quality of life and satisfaction with care among family caregivers of patients with recurrent or metastasized digestive cancer requiring palliative care. *Supportive Care in Cancer.* 2014;22(10):2687-2696.

23. van de Poll-Franse L, Nicolaije K, Vos M, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials*. 2011;12:256.
24. Nicolaije K, Ezendam N, Vos M, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology*. 2015;33(31):3550-3559.
25. de Rooij B, Ezendam N, Nicolaije K, et al. Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up - The ROGY care trial. *Gynecol Oncol*. 2017;S0090-8258(17)30162-2.
26. Arraras J, Greimel E, Sezer O, et al. An international validation study of the EORTC QLQ-INFO25 questionnaire: an instrument ti assess the information given to cancer patients. *Eur J Cancer*. 2010;46:2726-2738.
27. Bredart A, Bottomley A, Blazeby J, et al. An international prospective study of the EORTC cancer in-patient satisfaction with care measure (EORTC IN-PATSAT32). *Eur J Cancer*. 2005;41:2120-2131.
28. Broadbent E, Petrie K, Main J, Weinman J. The brief illness perception questionnaire. *J Psychosom Res*. 2006;60:631-637.
29. Zigmond A, Snaith R. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983;67:361-370.
30. Aaronson N, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85:365-376.
31. Twisk JW. *Applied multilevel analysis: a practical guide for medical researchers*. Cambridge University Press; 2006.
32. Peters SA, Bots ML, den Ruijter HM, et al. Multiple imputation of missing repeated outcome measurements did not add to linear mixed-effects models. *Journal of clinical epidemiology*. 2012;65(6):686-695.
33. Lowery WJ, Lowery AW, Barnett JC, et al. Cost-effectiveness of early palliative care intervention in recurrent platinum-resistant ovarian cancer. *Gynecologic oncology*. 2013;130(3):426-430.
34. Jones L, FitzGerald G, Leurent B, et al. Rehabilitation in advanced, progressive, recurrent cancer: a randomized controlled trial. *Journal of pain and symptom management*. 2013;46(3):315-325. e313.
35. Aldridge MD, Hasselaar J, Garralda E, et al. Education, implementation, and policy barriers to greater integration of palliative care: A literature review. *Palliative medicine*. 2016;30(3):224-239.
36. Lopez-Acevedo M, Lowery WJ, Lowery AW, Lee PS, Havrilesky LJ. Palliative and hospice care in gynecologic cancer: a review. *Gynecologic oncology*. 2013;131(1):215-221.
37. Elit LM, Charles C, Gafni A, Ranford J, Tedford-Gold S, Gold I. How oncologists communicate information to women with recurrent ovarian cancer in the context of treatment decision making in the medical encounter. *Health Expectations*. 2015;18(5):1066-1080.
38. Fitch M. Psychosocial management of patients with recurrent ovarian cancer: treating the whole patient to improve quality of life. *Semin Oncol Nurs*. 2003;19(3):40-53.

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Chapter 10

Summary of Results and General discussion

Summary of results

The central goal of this thesis was to understand the impact information provision has on (gynecological) cancer survivors and to use our findings to inform future survivorship care planning. The three overall aims were:

1. To assess the impact of survivorship care plans (SCPs) on patient-reported outcomes among ovarian and endometrial cancer survivors in daily clinical practice;
2. To understand the role illness peceptions play in the impact of SCPs;
3. To assess the need for information and care among (gynecological) cancer survivors across the cancer care continuum.

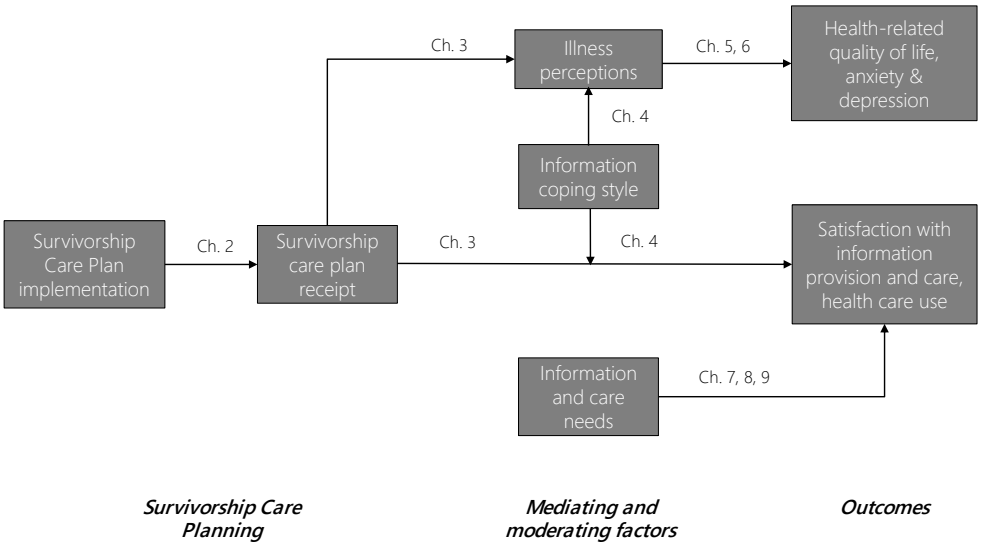

Figure 1: Conceptual framework of the effects of survivorship care plans and information and care needs on patient reported outcomes

Part I: the impact of SCPs on patient reported outcomes

As depicted in the conceptual framework presented in figure 1, we first assessed the degree of SCP receipt in the intervention arm of the ROGY Care Trial (N=178) and the factors associated with receipt of an SCP (**Chapter 2**). SCPs were generated for 90% of the patients in the trial arm, whereas 70% of the patients reported to have received one. Patients of an advanced age, patients with ovarian cancer, a distressed (type D) personality, and patients who completed the questionnaire a longer time after diagnosis, less often reported receipt of an SCP. These findings need to be taken into account when evaluating the effectiveness of SCPs on patient reported outcomes.

In our evaluation of the impact of SCPs on patient reported outcomes among ovarian cancer patients we accounted for receipt of an SCP. We compared all patients in the 'SCP Care' arm (N=61) to all patients in the 'Usual Care' arm (N=113; 'Intention-to-Treat' [ITT]). Likewise we compared patients who reported actual receipt of an SCP in the 'SCP Care' arm (N=40) to all patients in the 'Usual Care' arm (N=113; 'Per Protocol' [PP]) (**Chapter 3**). In both ITT and PP analyses, no beneficial effects of SCPs were found on satisfaction with information provision, satisfaction with care or health care use during the 2-year follow-up. SCPs did, however, increase threatening illness perceptions: they led to lower trust that the treatment would help cure the disease (6.7 vs. 7.5 on a 10-point scale, p<0.01). This is in line with previous findings among endometrial cancer patients that showed increased threatening illness perceptions: higher perceived impact of the disease, more concerns and more symptoms experienced due to the SCP. Therefore, SCPs may not be beneficial for all endometrial or ovarian cancer patients. They may, however, be beneficial for subgroups of patients.

Because individuals may respond differently to SCPs according to their information coping style, we further assessed whether the impact of SCPs differed between patients with an information-seeking ('monitoring') coping style compared to patients with an information-avoiding ('blunting') coping style (**Chapter 4**). Interestingly, patients with a monitoring coping style who received an SCP were more satisfied with the information received (73.9 vs. 63.9 on a 1-100 scale, p=0.04) and care received (74.5 vs. 69.2, p=0.03), while patients with a blunting coping style who received an SCP experienced more threatening illness perceptions, including a higher impact of the disease on their life (5.0 vs. 4.5, p=0.02) and a higher emotional impact of the disease (5.4 vs. 4.2, p=0.01). These results suggest that SCPs may be beneficial for subgroups of patients and reflect a need for tailored delivery of SCPs.

Part II: the role of illness perceptions

Prior chapters showed that SCPs may increase negative illness perceptions among endometrial and ovarian cancer patients, but it remained unclear whether this may ultimately be either beneficial or harmful for the patient. We showed that endometrial and ovarian cancer patients who experienced more threatening illness perceptions due to the SCP, had a lower HRQoL and more anxiety within 12 months after initial treatment (**Chapter 5**). Endometrial cancer patients who experienced more symptoms or concern due to the SCP reported worse social functioning (β=-0.82; P=0.01) and more fatigue, insomnia, pain and anxiety (β=0.58-0.86, P<0.05) within 12 months after initial treatment. Ovarian cancer patients who had lower trust that the treatment would cure their disease due to the SCP reported worse emotional functioning 6 months after treatment (β=0.27, P=0.02). These results suggest that SCPs may be harmful for patients at risk of developing threatening illness perceptions due to the SCP. Therefore, we should be aware of the potential negative consequences of SCPs.

The potential harm of threatening illness perceptions is further confirmed in a large sample of cancer survivors with various cancer diagnoses (**Chapter 6**). Survivors were categorized into a) illness perceptions consistent with prognosis ('realistic'), b) less threatening illness perceptions than expected based on prognosis ('optimistic'), and c) more threatening illness perceptions than expected based on prognosis ('pessimistic'). Compared to survivors with realistic illness perceptions, those with optimistic illness perceptions had a better HRQoL ($p<0.01$ on all EORTC QLQ-C30 scales) and lower mortality (HR=0.72, $p<0.01$), while those with pessimistic illness perceptions had a worse HRQoL ($p<0.01$ on all EORTC QLQ-C30 scales) and higher mortality (HR=1.52, $p<0.01$). These findings suggest that less threatening illness perceptions are most beneficial. However, illness perceptions may accurately reflect disease status regardless of prognosis, reflecting that additional support is needed for survivors with pessimistic illness perceptions.

Part III: information and care needs

In order to improve future survivorship care planning, we further sought to assess the information and care needs of cancer survivors across the cancer care continuum. With regard to survivorship care planning for patients recently diagnosed with a gynecological cancer at an American Medical Center, we assessed the perspectives of patients, caregivers and health care providers in a qualitative study (N=30) (**Chapter 7**). Almost all participants (95%) reported a desire for more information on how to address survivorship needs, specifically as they related to side effects (59%), follow-up schedule (32%), and psychological assistance (23%). Preferences for survivorship care planning largely differed across individuals and gynecological cancer types, with respect to content of the SCP, timing and mode of delivery. Hence, patients, caregivers and health care providers each expressed a need for survivorship care resources tailored to gynecological cancers, which requires multi-faceted, individualized survivorship care planning.

The need for individualized care for cancer survivors was further emphasized through a cluster analysis of survivorship care needs in a sample of American cancer survivors with various cancer types (N=292) (**Chapter 8**). We demonstrated that these needs can be broken down into 1) low needs (42%), 2) mainly physical needs (16%), 3) mainly psychological needs (20%) and 4) both physical and psychological needs (23%). Compared to cluster 1, patients in clusters 2, 3, and 4 were younger ($P<0.03$); those in clusters 3 and 4 had higher levels of psychological distress ($P<0.05$); and those in clusters 2 and 4 reported higher levels of fatigue ($P<0.05$). These findings show that needs among cancer survivors are prevalent, but a substantial group report low or no healthcare needs. This underscores the importance of both tailored information provision and accounting for differences in needs when testing interventions in survivorship care research.

As needs for survivorship care planning may change after recurrent disease, we additionally assessed the longitudinal impact of recurrent gynecological cancer on satisfaction with information provision and care. Therefore, we used data from the ROGY Care Trial as a prospective cohort (**Chapter 9**). During a 2-year follow-up, 25 patients with endometrial cancer (12%) and 64 patients with ovarian cancer (43%) had recurrent disease, of whom 9 endometrial and 26 ovarian cancer patients completed at least one questionnaire after their recurrence was determined. We showed that patients with recurrent endometrial or ovarian cancer were less satisfied with the interpersonal skills of the doctors, the exchange of information between caregivers, and care in general after diagnosis of a recurrence compared to before diagnosis of a recurrence as well as compared to patients without recurrent disease. Our findings reflect that patients with recurrent gynecological cancer are in need of care that is better tailored to their needs, suggesting a need for increased access to early palliative care.

General discussion

As a result of an ageing population, earlier diagnosis and improved treatment options, an increasing number of individuals worldwide live with or beyond a cancer diagnosis.[1-3] This growing group of cancer survivors faces difficulties in life after treatment, due to a host of physical and psychological effects of the cancer or cancer treatment.[4-6] In order to support cancer survivors to deal with issues related to survivorship, the American Institute of Medicine (IOM) recommended in 2006 that all cancer survivors should receive a survivorship care plan (SCP). This SCP should contain at least a treatment summary and a follow-up care plan that includes information about the long-term and late effects of the treatments received.[7] Although this recommendation was not evidence-based back in 2006, it has been widely supported and echoed outside of the United States, including the Netherlands.[8] However, the implementation and dissemination of SCPs has been slow and inconsistent.[9,10] Further, more than a decade after the IOM's recommendation, the evidence-base for the effectiveness of SCPs on patient reported outcomes is still inconclusive.

This thesis aimed to inform future survivorship care planning, by increasing the understanding of the impact of SCPs, the role of illness perceptions, as well as the need for information and care among (gynecological) cancer survivors.

MAIN FINDINGS

Receipt of survivorship care plans depends on patient characteristics

In the pragmatic ROGY Care Trial, oncology providers were free to choose who was providing the SCP (i.e. gynecologist, gynecologic oncologist or oncology nurse) and how much time was dedicated to counseling.[11] As a consequence of this pragmatic approach, a group of patients in the 'SCP Care' arm did not receive an SCP at all. More importantly, certain patients were less likely to report receipt of an SCP in the 'SCP Care' arm, including older patients, patients with ovarian cancer (as compared to endometrial cancer), a distressed (type D) personality and those who completed the questionnaire a longer time after diagnosis. For some patients, we are not sure if they really did not receive an SCP or forgot that they had received one, but we do know that SCPs were less often generated for patients with ovarian cancer compared with endometrial cancer. Thus, even in a trial, SCP delivery was inconsistent and dependent on patient characteristics. Although the potentially harmful effects of SCPs were unknown at the time of the trial, oncology providers may have - either intentionally or unintentionally – avoided providing SCPs to patients that might be at risk of harmful effects of SCPs. For instance, patients

with a distressed (type D) personality, who typically experience negative emotions and avoid social interactions[12], may be more likely to become worried by the information provided in the SCP. Therefore, oncology providers may have individualized information provision according to a patient's personality by choosing to provide or not to provide an SCP. Similarly, oncology providers may have avoided providing SCPs to older patients, because they generally have less need for information.[13,14] Yet, another explanation of the low self-reported SCP receipt in older patients or patients with a type D personality may be that they simply underreported the receipt, perhaps because of avoidance of the information,[15] dissatisfaction with information in general[15] or inaccurate recall.

Survivorship care plans may heal some, but hurt others

A main finding from the ROGY Care Trial reported in this thesis was that SCPs were - overall - not beneficial for ovarian cancer patients in terms of satisfaction with information provision and care, or health care use. These findings are in line with a previous publication from the ROGY Care Trial among endometrial cancer patients[16] and other trials that did not identify beneficial effects of SCPs on quality of life, psychological distress, or patient satisfaction with information and care, in various patient populations including breast[17-19], gynecological[20], colorectal[21] and prostate[22] cancer. However, a trial in a selected population of low-income breast cancer survivors did show increased implementation of recommended survivorship care.[23] Further, two trials combining SCPs with additional information packages or extensive counseling showed some improvements in perceived quality of care[21] and quality of life.[24]

Unlike other trials, we found that SCPs may be even harmful, by inducing threatening illness perceptions such as lower trust that the treatment would help cure the cancer. This in turn was associated with a decreased health-related quality of life (HRQoL) and increased anxiety within 12 months after diagnosis. Conversely, SCPs have earlier been found to decrease health worry in breast cancer survivors after 3 months, although this effect did not persist after 6 months.[19] However, the SCP provided in the latter trial was very concise and only summarized the key points, while our SCP was a rather extensive document that additionally contained explicit information about the chance of recurrence. Differences between SCP trials are important in the evaluation of the impact of SCPs and are therefore discussed in more detail under 'Methodological Considerations'.

Although SCPs do not seem beneficial in patient populations as a whole in current trials,[17-22] they may be valuable for subgroups of patients, such as patients with a monitoring coping style. However, SCPs seem to increase threatening illness perceptions in other patients such as those with a blunting coping style, which may result in decreased HRQoL and more anxiety. The harmful effects of threatening illness perceptions were further confirmed in this thesis by showing that threatening illness perceptions among cancer

survivors were associated with worse outcomes, even if they may seem 'realistic' with respect to a particular survivor's prognosis. Hence, 'realistic' illness perceptions, that may be obtained through explicit information about the disease and prognosis, may do more harm than good for some patients. It is a rather ethical question whether all survivors should be aware of all details of their disease, including all potential long-term and late effects and prognosis. On the contrary, our findings suggest that too much information may be detrimental for survivors' HRQoL. This may be particularly applicable to patients with a blunting coping style, who generally have lower levels of distress[25] that may be increased through extensive and explicit disease-related information such as SCPs. On the other hand, patients with a monitoring coping style generally have higher levels of distress, which may be decreased by adequate information about the disease,[25] while concise SCPs may leave them distressed and dissatisfied. Therefore, patients with a monitoring coping style may be in need of a more extensive SCP, like the one provided in our trial, while patients with a blunting coping style may prefer a more concise SCP that only summarizes the key points.

Stratification by information coping style is just an example of how delivery of SCPs could be tailored according to individual patients' needs. There are possibly many more patient characteristics that determine information needs and subsequently influence the need for and impact of an SCP. A previous publication from our trial showed that SCPs are also helpful for endometrial cancer patients who do not use the internet to look up medical information.[26] Further, a trial among low-income breast cancer survivors identified improvements in care delivery due to SCPs,[23] suggesting that socio-economic status may be another moderating factor of the impact of SCPs.

There is a wide variation in information and care needs

It is not completely surprising that SCPs have different effects on different patients, when we look further into their need for information and survivorship care services. This thesis showed that information and care needs largely differ across individuals, and also across the cancer care trajectory (i.e. before versus after diagnosis of a recurrence). A remarkable finding was that a considerable proportion of American cancer survivors (42%) had low or no information or care needs. Although a large part of current studies focused on distinct individual needs among cancer survivors[27-29], one other study using a similar cluster analysis identified an even larger cluster of breast cancer patients (63%) with little survivorship care needs.[30] The finding that not all survivors are in need of additional information or care was also described in our qualitative study among gynecological cancer survivors, and further aligns with the divergent responses to information among monitors and blunters in the ROGY Care Trial. Notably, these findings may explain why survivorship care interventions, such as SCPs, were not beneficial in unselected survivor populations.[17-22] Outcomes in these studies are inevitably diluted by the subgroup of patients that have very limited

needs and, subsequently, very little room for improvement. Therefore, we may need to focus on those individuals that do have remaining survivorship needs, when we want to improve survivors' outcomes.

Furthermore, survivors that do have unmet needs may not all have the same type of needs. Previous studies found that, overall, needs were highest with regard to physical symptoms and side-effects, practical assistance in daily living, and help with psychosocial problems such as anxiety and fear of recurrence.[27-29] This thesis showed that information and care needs are not universal across survivors and that subgroups of survivors can be identified that share similar needs, including those with physical needs, psychological needs, or both physical and psychological needs. Similar patterns of needs could be observed in our qualitative study among gynecological cancer patients within a year after treatment. Although these studies were in American patients of relatively high socio-economic status and few ethnic minorities, we expect that a certain extent of variation in survivorship care needs is generalizable to other populations. Unfortunately, we could not confirm whether information and care needs influence the impact of SCPs, because no baseline survivorship care needs assessment was included in our trial. If they do, we would need to tailor SCPs not only to the volume or detail of information that fit the information coping style, but also by the type of information that fits the type of the needs.

Another notable finding was that ovarian and endometrial cancer patients in the ROGY Trial were less satisfied with care after diagnosis of recurrent gynecological cancer compared with before their recurrence was diagnosed, as well as compared with patients without a recurrence. Patients with recurrent cancer were also less satisfied with information about the treatments and other services after their recurrence was diagnosed compared to before. Although the observed dissatisfaction may be explained by an overall disappointment about the disease outcome and additional hospital visits, it may alternatively suggest that the information and care for these patients is suboptimal. What type of information and care is needed for this population is yet unclear. Possibly, early palliative care, including early conversations about the goals and planning of care, support with coping such as redirecting hope, and assistance with management of symptoms, may meet the needs of patients with recurrent or progressive disease.[31] Thus, updated SCPs as provided in the ROGY Care Trial[11] may not sufficiently address the needs of patients with progressive or recurrent disease. Therefore, efforts are needed to improve the ongoing information and care for survivors when changes in disease status occur. More research in these patient populations is needed.

METHODOLOGICAL CONSIDERATIONS

The ROGY Care Plan differs from other survivorship care plans

When comparing results of the ROGY Care Trial to that of other SCP trials, it is important to consider any differences between the trials. An overview of the most relevant differences of current SCP trials is presented in Table 1. Most trials utilized SCP templates from the IOM,[32] American Society of Clinical Oncology (ASCO),[33] LIVESTRONG[34] or Journey Forward.[35] The latter one facilitates automatically generated SCPs using data from electronic patient charts similar to the ROGY Care plan, as used by Maly et al.[23] Although all SCP templates contain the elements recommended by the IOM[7], they considerably differ with respect to amount and detail of information. In the ROGY Care Trial, we provided a relatively extensive SCP that was up to 25 pages, depending on the treatments received. We included detailed information about potential long-term and late effects and, unlike other trials, elaborated on recurrence and survival rates. This may explain the negative effects we found on illness perceptions, quality of life and anxiety. Interestingly, Brothers et al. found that concise SCPs using ASCO's template of 1-3 pages decreased health worry after 3 months, although the effects did not persist after 6 months.[20] Hence, SCPs containing less detail and no prognostic information may be less harmful. Furthermore, Jefford et al. found that an SCP in combination with an additional information package containing a booklet and a DVD focusing on patient experiences may improve satisfaction with care[21], while Emery et al. did not find improved outcomes after providing additional information on tumor specific issues.[22] Perhaps the type of information (i.e. descriptions of patient experiences rather than factual information) plays an important role in the benefit for patients.

Another difference between the trials worth noting is the additional counseling that accompanied the SCP. Most trials scheduled an additional 30-60 minute consult to discuss the SCP, led by a nurse[17,18,21] or nurse and nutritionist.[19] Kvale et al. included even more extensive counseling using motivational interviewing techniques to develop a patient-owned SCP that contained strategies for follow-up, surveillance, symptom management and health goals.[24] In contrast, due to its pragmatic character in the ROGY Care Trial SCPs were discussed during a regularly scheduled consult, mostly when the results of initial surgery and the adjuvant treatment plan were discussed. Self-reported evaluation by the oncology providers in our trial showed that on average only 7 minutes were spent on discussing the SCP.[36] Thus, compared to other trials, the time for discussion in our trial was limited while the SCP was relatively extensive. Possibly, the harmful effects we found in our trial could be reduced by additional counseling, as this may help the patient to maintain hope and optimism while it also prepares for potential long-term and late effects.[37,38] However, whether SCPs accompanied with extensive counseling are beneficial for all patients remains yet unclear.

Importantly, detailed descriptions of the SCPs and counseling provided in current SCP trials were often lacking, which limits the possibility to compare research findings across trials. Therefore, future SCP trials should publish accurate protocol papers to enhance transparency and subsequently improve decision making based on trial outcomes.[39]

The inconsistent implementation reflects real-life clinical practice

An advantage of our pragmatic design was that implementation of SCPs in the intervention arm reflected 'real-life' clinical practice. Oncology providers were free to choose how the SCP was implemented, fitting in with the individual practice. They could choose who was providing the SCP (i.e. gynecologist, gynecologic oncologist or oncology nurse) and how much time was dedicated to counseling, provided that a minimum list of elements of the SCP was discussed. Further, our cluster-design allowed oncology providers to provide the same type of care to all patients in their practice (either 'SCP care' or 'Usual care'), which facilitated consistent implementation of SCPs for all patients in the 'SCP care' arm. Implementation was further facilitated by the ROGY system that supported automatically generated SCPs, which substantially limited the time needed to create an SCP and therefore helped to overcome one of the main barriers of implementation.[40,41] Despite these advantages, there were considerable differences in implementation across oncology providers. They were instructed to provide the SCP after initial surgery (6-8 weeks after diagnosis), but in some cases the SCP was provided after adjuvant treatment was finished (2-3 months after diagnosis). Further, some SCPs were rather extensively discussed with the patient, while in other cases SCPs were only sent by email and remaining questions could be answered by phone. We also showed in this thesis that between 10 and 30% of the patients reported not having received an SCP at all. Similarly, the trial from Jefford et al. reported that 24% of the patients did not receive counseling according to protocol, although all patients did receive an SCP.[21]

Whereas these inconsistencies may be interpreted as trial failure, they do reflect daily clinical practice, in which implementation of SCPs would likely be at least as inconsistent.[9,42] Therefore, evaluations of our pragmatic 'effectiveness' trial reflect the impact of SCPs when implemented in 'real-life' clinical practice. In contrast, in 'efficacy' trials where implementation is highly controlled, results may not be generalizable to the real world, such as when the SCP guideline is implemented.[43] However, more efforts may be needed towards implementation to optimize effectiveness in the real world.[44] Thus, our trial results do not fully show the potential benefit of SCPs when implementation were optimized. SCPs might possibly increase satisfaction if every patient received for example 30 minutes of counseling. Unfortunately, we did not assess all the parameters of the implementation process that may have influenced the effectiveness of SCPs, such as the time spent on discussing the SCP.

Table 1: Overview of randomized controlled trials (RCTs) assessing the impact of SCPs on patient reported outcomes

Trial	Cancer type (N)	SCP template (no. pages)	Additional information and counseling	Outcome measures	Measurement timepoint	Results (P<0.05)
Grunfeld, 2011	Breast (N=408)	IOM template (2-3)	Additional 30-min. nurse-led consult	Distress HRQoL Patient Satisfaction Quality of care	12 months	NS
Brothers, 2013	Gynecologic (N=121)	LIVESTRONG template (10-25)	Counseling during regular physician led consult	Quality of Care	Baseline	NS
Hershman, 2013	Breast (N=126)	ASCO template (1-3)	Additional 1-hour nurse- and nutritionist-led consult	Impact of Cancer Patient satisfaction Health worry	Baseline, 3 and 6 months	NS
Nicolaije, 2015	Endometrial (N=221)	Adapted IOM template (20-25)	Counseling during regular nurse/physician led consult	Satisfaction with information Satisfaction with care Illness perceptions Health care use	Baseline, 6 and 12 months	More information received, more concern, higher impact on life, more experienced symptoms, higher health care use
Boekhout, 2015 (extended results of Grunfeld, 2011)	Breast (N=408)	IOM template (2-3)	Additional 30-min nurse-led consult	Distress HRQoL Patient Satisfaction Continuity/coordination of Care	Baseline, 3, 6, 12, 18 and 24 months	NS
Jefford, 2016	Colorectal (N=217)	IOM template (2-3)	Information package and additional 1-hour nurse-led consult and telephone follow-up	Distress Unmet needs HRQoL Perceptions of Care	Baseline, 2 and 6 months	Higher satisfaction with care
Kvale, 2016	Breast (N=79)	Self-developed patient-owned SCP	Additional coach-led motivational interviewing session	HRQoL Distress Self-efficacy and self-management	Baseline and 3 months	Higher HRQoL
Maly, 2017	Breast (N=212)	Journey Forward template	Additional 1-hour nurse-led consult	Implementation of recommended care	Baseline to 12 months	Higher implementation of recommended care

Trial	Cancer type (N)	SCP template (no. pages)	Additional information and counseling	Outcome measures	Measurement timepoint	Results (P<0.05)
de Rooij, 2017	Ovarian (N=174)	Adapted IOM template (20-25)	Counseling during regular nurse/ physician led consult	Satisfaction with information Satisfaction with care Illness perceptions Health care use	Baseline, 6, 12 and 24 months	Lower treatment trust
Emery, 2017	Prostate (N=88)	Unknown	Additional information package, screening for distress and needs, follow-up care by general practitioner instead of hospital-based at 6 and 9 months	Distress HRQoL Unmet needs Patient satisfaction	Baseline, 3, 6, 12 months	NS

Outcome measures may be too insensitive or distal

Current trials evaluating the effectiveness of SCPs on PROs used various outcome measures, including patient satisfaction, psychological distress and HRQoL (Table 1). Similar to other trials[17-20,22] except for Jefford et al.[21], we did not find overall effects on satisfaction with information and care, which may be explained by insensitivity of the outcome measures. Patient satisfaction ratings are in large part influenced by the patient's personal preferences and expectations of care.[45] As a result, patient satisfaction measures are able to detect substantial discrepancies between patients' expectations and actual experience, for instance when care was extremely bad, but does not easily pick up changes when information or care is more or less in line with expectations.[45] Hence, in places where information and care provision is *not* extremely bad, it is hard to improve patient satisfaction ratings. This may explain the null findings on patient satisfaction in SCP trials, but may also explain why we did find improvements in satisfaction among patients with a monitoring coping style. Monitors typically have high expectations of information and care, resulting in a large discrepancy between expectations and actual experience. This suggests that patient satisfaction measures are useful in evaluations of SCPs among patients that have high expectations of care, but may be less likely to detect improvements among patients that are already relatively satisfied.

Further, most trials, including ours[17,20-22,24] except for Kvale et al.[24], did not find direct effects of SCPs on HRQoL. Interestingly, a recent qualitative study found that patients and oncology providers do not have expectations of SCPs to improve HRQoL.[46] Perhaps, HRQoL is a too distal outcome for effectiveness of SCPs. More proximal outcomes, such as the understanding of survivorship care issues[47] and care provider roles[47], self-management[46] and sense of control[46] may be more relevant in evaluations of SCPs. This may explain why we did find direct effects of SCPs on our most proximal outcome: illness perceptions. However, we also consider satisfaction with information and care as proximal outcome measures, which, in contrast, were not directly impacted by SCPs. As described earlier, this may be due to insensitivity of these outcome measures. The usefulness of alternative outcome measures in SCP trials, such as personal goal-setting[24] requires further research.

Some patient traits may be underrepresented

Selection bias is a common problem in trials and patient reported outcome research. Previous work showed that patients not participating in survey research are more likely to have a worse health status[48], age of either of both extremes[49] and a lower socio-economic status (SES)[49-51]. In the ROGY Care Trial, non-participating endometrial cancer patients had a lower SES, and ovarian cancer patients with higher cancer stages were more likely to be lost to follow-up, mostly due to death or ill-health, and were therefore underrepresented in our longitudinal analyses. Moreover, we showed that patients at an advanced age,

patients with ovarian cancer and a distressed (type D) personality less often reported receipt of an SCP, indicating that these patients are underrepresented in our evaluation of the effectiveness of SCPs. Particularly the underrepresentation of patients with a type D personality may have implications for our findings, as these patients may be more prone to distress due to the SCP.[15,52] Similarly, patients who avoid medical information (blunters) may be less likely to have participated in our trial because they do not want to be reminded of their cancer[53], while we demonstrate that these patients experience more threatening illness perceptions due to the SCP. Therefore, we may have underestimated the harmful effects of SCPs as a whole. The same reasoning may apply to the other studies included in this thesis. Considering that the unhealthy and distressed/vulnerable survivors may be underrepresented, we may provide a too optimistic perspective of the needs and outcomes of cancer survivors. As such, the proportion of survivors with information and care needs may be underestimated in our studies, and the poor health outcomes of survivors with pessimistic illness perceptions may be underestimated.

International differences impede the generalizability of results

This thesis includes studies that were conducted in the Netherlands as well as in the United States. Although challenges in survivorship care planning are reported worldwide, specific issues may depend on the national health care system and availability of survivorship care resources. In most European countries, and also in Canada and Australia, social health insurance is compulsory and managed by private health insurance companies, providing access to comprehensive cancer care for all citizens.[54] In contrast, in the United States there is no nation-wide health-care coverage, and not all aspects of cancer care are reimbursed by privately financed insurance companies or by the federally run Medicare program.[54] Particularly post-treatment cancer care lacks appropriate coordination across health care providers and payers.[55] Subsequently, there is a large variation in delivery of information and care to survivors across the United States. Therefore, particularly in American community practices where current information provision and survivorship care may be insufficient at some places, SCPs may have a greater impact on PROs. Maly et al. showed improvements in delivery of care in American community clinics serving Latina patients of low SES.[23] In contrast, in the ROGY Care Trial there was probably less room for improvement because existing information provision was already reasonably good at the time of the trial (inclusion years 2011-2014). However, a study conducted in 2008 among Dutch endometrial cancer patients diagnosed between 1999 and 2007 showed that 42% of the sample was dissatisfied with information provision.[56] Hence, information provision may have already improved during the past decade due to an increased focus on survivorship care. Notably, the two American studies included in this thesis were conducted at a large Academic Hospital with relatively high quality of care, perhaps already meeting a large part of survivors' needs. Thus, our finding that a substantial proportion of survivors has few unmet survivorship care needs may not be fully generalizable to other

clinical practices in the United States, but may be generalizable to other countries with similar quality of survivorship care.

FUTURE DIRECTIONS

There is a need for tailored delivery of survivorship care plans

We demonstrated in this thesis that there is a wide variation in information and care needs among (gynecological) cancer survivors, and that the impact of SCPs differs according to information coping style, suggesting a need for tailored delivery of survivorship care plans. The amount and detail ('intensity') of information provided in the SCP may need to be tailored according to the information coping style. Patients with an information-seeking coping style (monitors) have high information needs and may benefit from extensive SCPs, perhaps including explicit prognostic information, while patients with an information-avoiding coping style (blunters) may benefit from brief SCPs that only summarize the key points. Possibly, a simple set of screening questions could determine the need for extensive or concise information and triage survivors to appropriate SCPs. Perhaps, increased access to electronic medical records that include a summary of diagnosis and treatments received[57], could replace concise SCPs for those with limited information needs. However, those with high information needs (monitors) may need additional access to more extensive (web-based) SCPs.

A web-based SCP may be useful to tailor the content of information according to survivors' information and care needs. We showed that these needs may be broken down into 1) low needs, 2) physical needs, 3) psychological needs or 4) both physical and psychological needs. Providing distinct 'modules' of information according to reported needs may be a viable strategy to meet those specific needs, and they could be adjusted according to (gynecological) cancer type. Further research is required to develop an efficient screening tool to identify survivors' needs and to develop tailored (web-based) SCPs to meet those needs. Additionally, the type of information, such as descriptions of patient experiences rather than factual information[21] may further meet survivors' needs.

Importantly, a certain degree of counseling may be needed to accompany with the SCP. The fact that counseling in our trial was limited[36] while our SCPs were extensive and included explicit prognostic information, may explain the harmful effects we found on illness perceptions, quality of life and anxiety. The few trials that did find beneficial effects of SCPs included an additional nurse- or coach-led consult to discuss the content of the SCP.[21,23,24] This consult can even be used to develop a patient-owned SCP as demonstrated by Kvale et al., focusing on self-management.[24] Therefore, even if the SCP is provided online, additional oral information may be required when the SCP is accessed for the first time.

Further, according to the preferences of most patients and caregivers in our qualitative study, tailored SCPs should be provided after the conclusion of treatment. In the ROGY Care Trial, however, patients received the SCP after initial surgery, but before the start of adjuvant treatment. The IOM originally recommended that the SCP should be a two-part tool, in which the treatment plan is provided right after diagnosis, while the follow-up care plan is provided after treatment.[32] Although the SCP in our trial could be updated when changes in disease status, treatments or oncology providers occurred, this may not have been sufficient to address changing needs over time. We demonstrated that satisfaction with information and care changed after diagnosis of a recurrence, suggesting that additional support is required when changes in diagnosis or treatments occur. A dynamic web-based SCP could provide additional modules of information that specifically address issues related to recurrent or progressive disease.

More intensive interventions may benefit survivors with highest needs

We suggested that the wide variation in information and care needs among cancer survivors could be addressed by tailoring the 'intensity' of the information: patients with higher needs may require a higher 'intensity' of information and support (i.e. extensive SCPs), while those with lower needs may require less (concise SCPs). Herein SCPs could be part of a 'stepped-care' approach, which starts with a low intensity intervention, while only the patients with remaining needs are referred to the next step offering a more intensive intervention.[58] For example, as a first step, all cancer survivors could be provided with concise SCPs or access to treatment summaries in electronic medical record systems, accompanied by a (nurse-led) consult assessing the need for further information and support. Currently, in the Netherlands, a distress thermometer is used as a screening tool for psychological needs[59], which could be used as a starting point for further development of a more comprehensive needs assessment tool. As a second step in the 'stepped-care' model, only those patients with remaining information or care needs could be provided with more extensive, tailored web-based SCPs and additional counseling if needed. As a third step, the individuals with remaining needs could be provided with more intensive support such as psychological therapy or medication.

Alternatively, as a second step, web-based self-management tools could be provided such as the Kanker Nazorg Wijzer (Cancer Aftercare Guide; KNW) or the breast cancer e-health intervention (BREATH). The KNW provides personalized information and support on psychosocial and lifestyle issues, based on responses to a screening questionnaire, and further serves as a needs assessment for more intensive care as the next step in the stepped-care model.[60] The KNW improved HRQoL at 6 months from baseline, but the participation rate was relatively low (40%), suggesting that non-participants did not have a need for such an extensive online management tool.[61] However, another web-based self-management tool (BREATH) had high participation rates (89%) and helped

to reduce distress among breast cancer survivors.[62] Possibly, the combination of less intensive interventions such as brief SCPs for all cancer survivors and more intensive e-health interventions for selected survivors with remaining needs, could be an efficient means to address the needs of cancer survivors. In this respect, information provision and support for survivors could be based on risk stratification according to needs, similar to the method applied in individualized follow-up.[63] However, face-to-face counseling may be required for all survivors as a means to screen for information and care needs. Further research on this topic is warranted.

Our results may also apply to other types of information provision

A disturbing finding reported in this thesis is that, in some patients, SCPs increased threatening illness perceptions, resulting in a lower health-related quality of life and more anxiety. These illness perceptions, including a higher impact of the disease on life, more concerns about the disease, more symptoms experienced and lower trust in the treatment, may be explained by the detailed list of long-term and late effects and explicit prognostic information included in the SCP, and limited counseling to discuss this information. Importantly, our findings suggest that we should be careful in providing such explicit information that may be perceived as threatening, which may also apply to other types of information provision. For example, (web-based) tools to estimate individual patients' recurrence risk or survival based on cancer registry data (nomogram)[64,65] may increase worry when they are accessible to patients and no appropriate counseling is provided. Therefore, these tools may require careful evaluation of the potentially harmful effects before they are made widely available to patients. On the other hand, such information provision tools may be mostly used by a self-selected group of patients with an information-seeking coping style and high information needs, which would limit the harmful effects.

The translation from research findings to practical guidelines is slow

Since the recommendation of the IOM to provide SCPs to all cancer survivors in 2006, a large number of studies sought to evaluate the benefits of SCPs. Although RCTs were scarce in the first years after the recommendation, they evolved when SCPs became a care standard in the American Commission of Cancer (CoC) affiliated centers (70% of all U.S. cancer centers) in 2015.[66] The CoC aimed for a 10% SCP receipt in that year, and 25%, 50% and 75% in the following years respectively. However, results of emerging trials and non-randomized studies evaluating the impact of SCPs on PROs and health care delivery do not fully support this guideline, as summarized in a recently published review by Jacobsen et al.[47] Although methodological limitations and inconsistencies in current SCP trials limit the possibility to draw definite conclusions about the effectiveness of SCPs, current evidence does not provide convincing support for the benefit of SCPs either. Despite the many null findings to date, the CoC does not want to abandon their care

standard, mainly because it helped cancer programs to get survivorship on the radar.[66] Also the IOM, ASCO and the American Cancer Society keep supporting SCPs to date.[66] Similarly, in the Netherlands, the guideline for implementation of SCPs was published in 2011 (*Richtlijn Herstel na Kanker*)[67] and has not been changed since. Changes in current SCP guidelines, such as tailored delivery of SCPs based on needs assessments during a consult, would likely receive more support among stakeholders than abolishment of the entire guideline. Future research is required to explore efficient and effective means to tailor SCPs to survivors' information and care needs in order to achieve improvements in current SCP guidelines.

CONCLUDING REMARKS

More than a decade after the recommendation of the IOM to implement SCPs for all cancer survivors,[32] the evidence for the effectiveness in unselected patient populations is still limited.[68] However, (extensive) SCPs may be beneficial for subgroups of survivors, such as those with an information-seeking coping style, while they may be less beneficial and perhaps even harmful for those with an information-avoiding coping style, suggesting a need for tailored delivery of SCPs. More comprehensive (nurse-led) counseling may be needed to discuss the information provided in the SCP, to support patients' self-management skills and to screen for remaining information and care needs. Further research is needed to develop (web-based) tools to tailor information provision to survivors' needs with respect to the level of detail, content and type of information, in order to improve current SCP guidelines and subsequently improve survivorship care planning.

REFERENCES

1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. *Cancer Epidemiology and Prevention Biomarkers*. 2016;25(1):16-27.
2. Registry" NC. Incidentie alle tumoren. *Cijfers over Kanker* 2018; www.cijfersoverkanker.nl.
3. KWF. *Kanker in Nederland tot 2020, Trends en Prognoses*. 2011.
4. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *The International Journal of Psychiatry in Medicine*. 2010;40(2):163-181.
5. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. *Cancer*. 2008;112(S11):2577-2592.
6. Wu H-S, Harden JK. Symptom burden and quality of life in survivorship: a review of the literature. *Cancer nursing*. 2015;38(1):E29-E54.
7. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
8. Netherlands HCot. *Follow-up in oncology. Identify objectives, substantiate actions*. The Hague: Health Council of the Netherlands;2007.
9. Birken SA, Deal AM, Mayer DK, Weiner BJ. Following through: the consistency of survivorship care plan use in United States cancer programs. *Journal of cancer education : the official journal of the American Association for Cancer Education*. Dec 2014;29(4):689-697.
10. Birken SA, Deal AM, Mayer DK, Weiner BJ. Determinants of survivorship care plan use in US cancer programs. *Journal of cancer education : the official journal of the American Association for Cancer Education*. Dec 2014;29(4):720-727.
11. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials*. 2011;12:256.
12. Denollet J. DS14: standard assessment of negative affectivity, social inhibition, and Type D personality. *Psychosomatic medicine*. 2005;67(1):89-97.
13. Thompson AG, Sunol R. Expectations as determinants of patient satisfaction: concepts, theory and evidence. *International journal for quality in health care*. 1995;7(2):127-141.
14. Ganz PA, Schag CC, Heinrich RL. The psychosocial impact of cancer on the elderly: a comparison with younger patients. *Journal of the American Geriatrics Society*. 1985;33(6):429-435.
15. Husson O, Denollet J, Oerlemans S, Mols F. Satisfaction with information provision in cancer patients and the moderating effect of Type D personality. *Psycho-Oncology*. 2013;22(9):2124-2132.
16. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology*. 2015;33(31):3550-3559.
17. Grunfeld E, Julian JA, Pond G, et al. Evaluating survivorship care plans: results of a randomized, clinical trial of patients with breast cancer. *Journal of Clinical Oncology*. 2011;29(36):4755-4762.
18. Boekhout AH, Maunsell E, Pond GR, et al. A survivorship care plan for breast cancer survivors: extended results of a randomized clinical trial. *Journal of Cancer Survivorship*. 2015;9(4):683-691.
19. Hershman DL, Greenlee H, Awad D, et al. Randomized controlled trial of a clinic-based survivorship intervention following adjuvant therapy in breast cancer survivors. *Breast cancer research and treatment*. 2013;138(3):795-806.
20. Brothers BM, Easley A, Salani R, Andersen BL. Do survivorship care plans impact patients' evaluations of care? A randomized evaluation with gynecologic oncology patients. *Gynecologic oncology*. 2013;129(3):554-558.
21. Jefford M, Gough K, Drosdowsky A, et al. A randomized controlled trial of a nurse-led supportive care package (SurvivorCare) for survivors of colorectal cancer. *The oncologist*. 2016;21(8):1014-1023.
22. Emery JD, Jefford M, King M, et al. ProCare Trial: a phase II randomized controlled trial of shared care for follow-up of men with prostate cancer. *BJU international*. 2017;119(3):381-389.

23. Maly RC, Liang L-J, Liu Y, Griggs JJ, Ganz PA. Randomized Controlled Trial of Survivorship Care Plans Among Low-Income, Predominantly Latina Breast Cancer Survivors. *Journal of Clinical Oncology.* 2017;35(16):1814-1821.
24. Kvale EA, Huang CS, Meneses KM, et al. Patient-centered support in the survivorship care transition: Outcomes from the Patient-Owned Survivorship Care Plan Intervention. *Cancer.* Oct 15 2016;122(20):3232-3242.
25. Miller SM, Mangan CE. Interacting effects of information and coping style in adapting to gynecologic stress: should the doctor tell all? *Journal of personality and social psychology.* 1983;45(1):223.
26. Nicolaije KA, Ezendam NP, Pijnenborg JM, et al. Paper-Based Survivorship Care Plans May be Less Helpful for Cancer Patients Who Search for Disease-Related Information on the Internet: Results of the Registrationsystem Oncological Gynecology (ROGY) Care Randomized Trial. *Journal of medical Internet research.* 2016;18(7).
27. Geller BM, Vacek PM, Flynn BS, Lord K, Cranmer D. What are cancer survivors' needs and how well are they being met? *The Journal of family practice.* Oct 2014;63(10):E7-16.
28. Harrison JD, Young JM, Price MA, Butow PN, Solomon MJ. What are the unmet supportive care needs of people with cancer? A systematic review. *Supportive Care in Cancer.* 2009;17(8):1117-1128.
29. Kent EE, Arora NK, Rowland JH, et al. Health information needs and health-related quality of life in a diverse population of long-term cancer survivors. *Patient education and counseling.* 2012;89(2):345-352.
30. Aranda S, Schofield P, Weih L, et al. Mapping the quality of life and unmet needs of urban women with metastatic breast cancer. *European journal of cancer care.* 2005;14(3):211-222.
31. Hoerger M, Greer JA, Jackson VA, et al. Defining the Elements of Early Palliative Care That Are Associated With Patient-Reported Outcomes and the Delivery of End-of-Life Care. *Journal of Clinical Oncology.* 2018;36(11):1096-1102.
32. Hewitt M, Ganz P. Implementing cancer survivorship care planning: workshop summary. 2007.
33. ASCO ASoCO. Survivorship Care Planning Tools. *Survivorship Compendium* 2018; https://www.asco.org/practice-guidelines/cancer-care-initiatives/prevention-survivorship/survivorship-compendium. Accessed March 13, 2018, 2018.
34. Oncolink. Oncolife Survivorship Care Plen. *Livestrong Care Plan* 2018; http://www.livestrongcareplan.org/.
35. Forward" J. Cancer Care Plan Builder. *Provider Tools* 2018; https://www.journeyforward.org/professionals/survivorship-care-plan-builder. Accessed 16-05-2018, 2018.
36. Nicolaije KA, Ezendam NP, Vos MC, Pijnenborg JM, van de Poll-Franse LV, Kruitwagen RF. Oncology providers' evaluation of the use of an automatically generated cancer survivorship care plan: longitudinal results from the ROGY Care trial. *Journal of cancer survivorship : research and practice.* Jun 2014;8(2):248-259.
37. Clayton JM, Hancock K, Parker S, et al. Sustaining hope when communicating with terminally ill patients and their families: a systematic review. *Psycho-oncology.* Jul 2008;17(7):641-659.
38. Hancock K, Clayton JM, Parker SM, et al. Truth-telling in discussing prognosis in advanced life-limiting illnesses: a systematic review. *Palliative medicine.* 2007;21(6):507-517.
39. Dal-Ré R, Bracken MB, Ioannidis JP. Call to improve transparency of trials of non-regulated interventions. *BMJ: British Medical Journal (Online).* 2015;350.
40. Dulko D, Pace CM, Dittus KL, et al. Barriers and facilitators to implementing cancer survivorship care plans. *Oncology nursing forum.* Nov 2013;40(6):575-580.
41. Mayer DK, Birken SA, Check DK, Chen RC. Summing it up: an integrative review of studies of cancer survivorship care plans (2006-2013). *Cancer.* Apr 1 2015;121(7):978-996.
42. Birken SA, Mayer DK, Weiner BJ. Survivorship care plans: prevalence and barriers to use. *Journal of cancer education : the official journal of the American Association for Cancer Education.* Jun 2013;28(2):290-296.
43. Singal AG, Higgins PD, Waljee AK. A primer on effectiveness and efficacy trials. *Clinical and translational gastroenterology.* 2014;5(1):e45.
44. Mayer DK, Birken SA, Chen RC. Avoiding Implementation Errors in Cancer Survivorship Care Plan Effectiveness Studies. *Journal of Clinical Oncology.* 2015:JCO. 2015.2062. 6937.

45. Sitzia J, Wood N. Patient satisfaction: a review of issues and concepts. *Social science & medicine.* 1997;45(12):1829-1843.
46. Birken SA, Urquhart R, Munoz-Plaza C, et al. Survivorship care plans: are randomized controlled trials assessing outcomes that are relevant to stakeholders? *Journal of Cancer Survivorship.* 2018:1-14.
47. Jacobsen PB, DeRosa AP, Henderson TO, et al. Systematic Review of the Impact of Cancer Survivorship Care Plans on Health Outcomes and Health Care Delivery. *Journal of Clinical Oncology.*0(0):JCO.2018.2077.7482.
48. Perneger TV, Chamot E, Bovier PA. Nonresponse bias in a survey of patient perceptions of hospital care. *Medical care.* 2005;43(4):374-380.
49. Downing A, Morris EJ, Richards M, et al. Health-related quality of life after colorectal cancer in England: a patient-reported outcomes study of individuals 12 to 36 months after diagnosis. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Feb 20 2015;33(6):616-624.
50. Kjaer T, Johansen C, Andersen E, et al. Do we reach the patients with the most problems? Baseline data from the WebCan study among survivors of head-and-neck cancer, Denmark. *Journal of cancer survivorship : research and practice.* Apr 2016;10(2):251-260.
51. Shen M, Cozen W, Huang L, et al. Census and geographic differences between respondents and nonrespondents in a case-control study of non-Hodgkin lymphoma. *American journal of epidemiology.* 2008;167(3):350-361.
52. Mols F, Denollet J, Kaptein AA, Reemst PH, Thong MS. The association between Type D personality and illness perceptions in colorectal cancer survivors: a study from the population-based PROFILES registry. *Journal of psychosomatic research.* 2012;73(3):232-239.
53. Miller SM. Monitoring versus blunting styles of coping with cancer influence the information patients want and need about their disease. Implications for cancer screening and management. *Cancer.* 1995;76(2):167-177.
54. Jefford M, Rowland J, Grunfeld E, Richards M, Maher J, Glaser A. Implementing improved post-treatment care for cancer survivors in England, with reflections from Australia, Canada and the USA. *British journal of cancer.* 2013;108(1):14.
55. Rowland JH, Kent EE, Forsythe LP, et al. Cancer survivorship research in Europe and the United States: where have we been, where are we going, and what can we learn from each other? *Cancer.* 2013;119(S11):2094-2108.
56. Nicolaije KA, Husson O, Ezendam NP, et al. Endometrial cancer survivors are unsatisfied with received information about diagnosis, treatment and follow-up: a study from the population-based PROFILES registry. *Patient education and counseling.* Sep 2012;88(3):427-435.
57. Tevaarwerk AJ, Wisinski KB, Buhr KA, et al. Leveraging electronic health record systems to create and provide electronic cancer survivorship care plans: a pilot study. *Journal of oncology practice.* 2014;10(3):e150-e159.
58. Bower P, Gilbody S. Stepped care in psychological therapies: access, effectiveness and efficiency: narrative literature review. *The British Journal of Psychiatry.* 2005;186(1):11-17.
59. Willems RA, Bolman CA, Mesters I, Kanera IM, Beaulen AA, Lechner L. The Kanker Nazorg Wijzer (Cancer Aftercare Guide) protocol: the systematic development of a web-based computer tailored intervention providing psychosocial and lifestyle support for cancer survivors. *BMC cancer.* 2015;15(1):580.
60. Willems RA, Bolman CA, Mesters I, Kanera IM, Beaulen AA, Lechner L. Short-term effectiveness of a web-based tailored intervention for cancer survivors on quality of life, anxiety, depression, and fatigue: randomized controlled trial. *Psycho-oncology.* 2017;26(2):222-230.
61. van den Berg SW, Gielissen MF, Custers JA, van der Graaf WT, Ottevanger PB, Prins JB. BREATH: web-based self-management for psychological adjustment after primary breast cancer—Results of a multicenter randomized controlled trial. *Journal of Clinical Oncology.* 2015;33(25):2763-2771.
62. Leeson SC, Beaver K, Ezendam NPM, et al. The future for follow-up of gynaecological cancer in Europe. Summary of available data and overview of ongoing trials. *European journal of obstetrics, gynecology, and reproductive biology.* Mar 2017;210:376-380.

63. Witteveen A, Vliegen IM, Sonke GS, Klaase JM, IJzerman MJ, Siesling S. Personalisation of breast cancer follow-up: a time-dependent prognostic nomogram for the estimation of annual risk of locoregional recurrence in early breast cancer patients. *Breast cancer research and treatment.* 2015;152(3):627-636.
64. Peeters KC, Kattan MW, Hartgrink HH, et al. Validation of a nomogram for predicting disease-specific survival after an R0 resection for gastric carcinoma. *Cancer.* 2005;103(4):702-707.
65. Miller NS. The Commission on Cancer's survivorship care plan standard: Implementation is underway. American Society of Clinical Oncology; 2017.
66. Oncoline. Herstel na Kanker, Landelijke Richtlijn, versie 1.0. www.oncoline.nl: Oncoline; 2011.
67. Jacobsen PB. DA, Henderson TO., Mayer D., Moskowitz CS., Paskett ED., Rowland JH. Impact of cancer survivorship care plans (SCPs) on health outcomes and health care delivery: A systematic review. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* 2018;36, 2018 (suppl 7S; abstract 2).

Nederlandse samenvatting

Dutch summary

INLEIDING

Het aantal mensen dat kanker heeft of heeft gehad neemt wereldwijd toe, door vergrijzing van de bevolking, vroegere opsporing en betere behandelingen.[1-3] In 2017 waren er in Nederland al bijna 800 duizend (ex-)patiënten met kanker en er wordt verwacht dat dit aantal al in 2025 is gestegen naar één miljoen.[3,4] Deze (ex-)patiënten krijgen vaak te maken met verschillende lichamelijke en psychologische gevolgen van de kanker of de behandelingen die zij hebben gehad. Veelvoorkomende problemen zijn (ernstige) vermoeidheid, slaapproblemen, cognitieve beperkingen, seksuele problemen, angst voor terugkeer van de kanker en depressie.[5,6]

Pas sinds de laatste decennia is er wereldwijd meer aandacht voor de problemen van mensen die kanker hebben of hebben gehad. Zo heeft het Amerikaanse Instituut voor Geneeskunde (*Institute of Medicine,* IOM) in 2006 het advies uitgebracht om alle patiënten na de kankerbehandeling te voorzien van een 'zorgplan'.[7] Dit zorgplan bevat schriftelijke informatie over de diagnose van de patiënt, de behandelingen die hij of zij heeft ondergaan, mogelijke korte- en langetermijngevolgen van de behandelingen en leefstijladviezen.[7] Sinds 2007 adviseert ook de Nederlandse Gezondheidsraad zorgplannen voor iedereen die in Nederland voor kanker is behandeld. [8] Ten tijde van dit advies was er nog nauwelijks wetenschappelijk onderzoek gedaan naar de effectiviteit van zorgplannen, bijvoorbeeld naar de tevredenheid onder patiënten en zorgverleners. Inmiddels, meer dan 10 jaar later, zijn er wereldwijd een beperkt aantal gerandomiseerde studies gedaan en die laten weinig overtuigend bewijs zien van de baten van het zorgplan.[9]

In 2011 is in Nederland de ROGY Care Studie uitgevoerd om te onderzoeken wat de effectiviteit is van zorgplannen bij patiënten met baarmoeder- en eierstokkanker gedurende twee jaar na diagnose.[10] Twaalf ziekenhuizen in Zuid-Nederland werden gerandomiseerd naar het verlenen van zorgplannen óf naar het verlenen van de gebruikelijke zorg aan al hun baarmoeder- en eierstokkankerpatiënten. Baarmoeder- en eierstokkanker zijn de twee meest voorkomende gynaecologische tumoren. In Nederland kregen in 2017 bijna 2.000 vrouwen de diagnose baarmoederkanker en 1.300 de diagnose eierstokkanker. Eierstokkanker is de meest dodelijke van de twee; slechts 38% van de eierstokkankerpatiënten is 5 jaar na diagnose nog in leven, terwijl ongeveer 80% van de baarmoederkankerpatiënten dan nog in leven is. Veelvoorkomende problemen die patiënten ervaren na de behandeling van baarmoeder- of eierstokkanker zijn pijn, post-menopauzale klachten, seksuele problemen, blaas- en darmproblemen, onvruchtbaarheid, neuropathie en vermoeidheid.[11-13]

Eerdere resultaten van de ROGY Care Studie bij baarmoederkankerpatiënten lieten zien dat het zorgplan geen invloed had op de tevredenheid met de informatievoorziening

en zorg onder de patiënten.[14] Verrassend was dat baarmoederkankerpatiënten die een zorgplan hadden ontvangen zich juist meer zorgen maakten, meer emotionele gevolgen van de ziekte ondervonden en meer lichamelijke klachten. Ook namen ze vaker contact op met hun huisarts in verband met deze problemen.[14] Het bleef echter nog onduidelijk of deze gevolgen van het verstrekken van een zorgplan schadelijk zijn voor deze patiënten of misschien juist wel gunstig. Daarnaast bleef onduidelijk wat het effect van zorgplannen is bij eierstokkankerpatiënten.

DOEL VAN DIT PROEFSCHRIFT

De drie overkoepelende doelen van dit proefschrift zijn:

1. Het onderzoeken van de effecten van zorgplannen op patiënt-gerapporteerde uitkomsten bij eierstok- en baarmoederkankerpatiënten in de dagelijkse klinische praktijk;
2. Het begrijpen van de rol die ziektepercepties spelen in de impact van een zorgplan;
3. Het onderzoeken van de informatie- en zorgbehoeften van mensen die een (gynaecologische) kanker hebben, hebben gehad of bij wie de kanker is teruggekeerd.

BELANGRIJKSTE BEVINDINGEN

Deel I: de invloed van zorgplannen op patiënt-gerapporteerde uitkomsten

In **hoofdstuk 2** van dit proefschrift evalueren we hoeveel eierstok- en baarmoederkankerpatiënten in de interventiegroep van de ROGY Care Trial (N=178) een zorgplan hebben ontvangen en wie dat waren. We laten zien dat er voor 90% van deze patiënten een zorgplan werd gegenereerd in het registratiesysteem ROGY, terwijl maar 70% van de patiënten aangeeft daadwerkelijk een zorgplan te hebben ontvangen. Oudere Patiënten, patiënten die een negatieve en sociaal geremde (type D) persoonlijkheid hebben, en patiënten die de vragenlijst later invulden, rapporteerden vaker dat zij geen zorgplan hadden ontvangen. Het is belangrijk om deze bevindingen mee te nemen in de interpretatie van de effectiviteit van het zorgplan in de volgende hoofdstukken.

In **hoofdstuk 3** beschrijven we de effecten van zorgplannen op de tevredenheid met informatievoorziening en zorg, op ziektepercepties en op zorggebruik van eierstokkankerpatiënten gedurende twee jaar na diagnose. Om rekening te houden met het gegeven dat niet alle patiënten in de interventiegroep een zorgplan hadden ontvangen, hebben we niet alleen de uitkomsten vergeleken van alle patiënten in de interventiegroep (N=61) met alle patiënten in de controlegroep (N=113; 'Intention-to-treat' [ITT] analyse), maar hebben

we ook een vergelijking gemaakt van de patiënten in de interventiegroep die aangaven een zorgplan te hebben ontvangen (N=40) met de patiënten in de controlegroep (N=113; 'per-protocol-analyse' [PP]). In beide analyses zagen we dat zorgplannen geen gunstig effect hadden op de tevredenheid over informatievoorziening en zorg. We zagen wel dat zorgplannen de ziektepercepties verhoogden: patiënten kregen namelijk minder vertrouwen in de behandeling door het lezen van het zorgplan (6.7 versus 7.5 op een 10-puntsschaal, ITT analyse). Deze resultaten zijn vergelijkbaar met eerdere bevindingen van de ROGY Care Studie bij baarmoederkankerpatiënten. Blijkbaar hebben niet alle baarmoeder- en eierstokkankerpatiënten, maar wellicht wel subgroepen van patiënten, baat bij een zorgplan.

Uit de literatuur blijkt dat mensen verschillend reageren op en omgaan met medische informatie; ze hebben verschillende informatie-coping-stijlen. In **hoofdstuk 4** evalueren we of het effect van zorgplannen verschillend is voor patiënten met een informatie-zoekende of met een informatie-vermijdende coping-stijl. We laten zien dat patiënten met een informatie-zoekende coping-stijl die een zorgplan ontvingen, meer tevreden waren met de informatievoorziening (73.9 vs. 63.9, schaal 1-100) en zorg (74.5 vs. 69.2, schaal 1-100), terwijl patiënten met een informatie-vermijdende coping-stijl die een zorgplan hadden ontvangen, meer bedreigende ziektepercepties ervaarden, zoals de invloed van de ziekte op hun leven (5.0 vs. 4.5, schaal 1-10) en de emotionele invloed van de ziekte (5.4 vs. 4.2, schaal 1-10), ten opzichte van degenen die geen zorgplan hadden ontvangen. Deze resultaten tonen aan dat het samenstellen van een gepersonaliseerd zorgplan wellicht uitkomst kan bieden.

Deel II: de rol van ziektepercepties

Eerdere hoofdstukken lieten zien dat zorgplannen de ziektepercepties van baarmoeder- en eierstokkankerpatiënten kunnen verhogen. Het bleef echter onduidelijk of deze verhoogde ziektepercepties schadelijk zijn voor patiënten of misschien juist wel gunstig op de lange termijn. **Hoofdstuk 5** laat zien dat patiënten die meer bedreigende ziektepercepties ervaarden door het zorgplan, ook een lagere kwaliteit van leven en meer angst ervaarden in de eerste twaalf maanden na de behandeling. Baarmoederkankerpatiënten die zich meer zorgen maakten over de ziekte of meer klachten hadden, rapporteerden een slechter sociaal functioneren, meer vermoeidheid, slapeloosheid, pijn en angst in de twaalf maanden na de behandeling. Eierstokkankerpatiënten die door het zorgplan minder vertrouwen in de behandeling hadden, rapporteerden een slechter emotioneel functioneren in de zes maanden na de behandeling. Deze resultaten laten zien dat zorgplannen zelfs schadelijk kunnen zijn voor sommige patiënten en dat we ons bewust moeten zijn van de mogelijk negatieve gevolgen.

De mogelijk negatieve gevolgen van bedreigende ziektepercepties worden nader beschreven in **hoofdstuk 6**, in een studie onder mensen met verschillende kankerdiagnoses (N=2,457). Deze (ex-)patiënten werden verdeeld in de volgende groepen: zij met a) ziektepercepties die in lijn zijn met de prognose ('realistisch'), b) ziektepercepties die minder bedreigend zijn dan verwacht op grond van de prognose ('optimistisch') en c) ziektepercepties die meer bedreigend zijn dan verwacht op grond van de prognose ('pessimistisch'). In vergelijking met degenen met realistische ziektepercepties, hadden degenen met optimistische ziektepercepties een beduidend hogere kwaliteit van leven en een betere overleving, terwijl degenen met pessimistische ziektepercepties een beduidend lagere kwaliteit van leven hadden en een slechtere overleving. Deze resultaten wijzen erop dat pessimistische ziektepercepties het minst gunstig zijn en dat passende zorg nodig is om de kwaliteit van leven van (ex-)patiënten met pessimistische ziektepercepties te verbeteren.

Deel III: informatie- en zorgbehoeften

Ten behoeve van de zorg voor (ex-)kankerpatiënten hebben we verder onderzoek gedaan naar de informatie- en zorgbehoeften van mensen die kanker hebben, hebben gehad, of terugkerende kanker (een recidief) hebben. **Hoofdstuk 7** beschrijft een studie onder Amerikaanse patiënten die recent zijn gediagnostiseerd met een gynaecologische kanker en de behandeling hebben afgerond, maar ook hun naasten en zorgverleners. In deze kwalitatieve studie gaven bijna alle patiënten en naasten aan dat zij behoefte hadden aan aanvullende informatie na de behandeling, voornamelijk over bijwerkingen van de behandelingen, het nacontroleschema en psychologische hulpverlening. De behoefte aan een zorgplan verschilde sterk tussen individuen en naar gelang de gynaecologische tumorsoort, met betrekking tot de inhoud van het zorgplan en het moment en de manier van verstrekking. Zowel patiënten, naasten als zorgverleners uitten de behoefte aan tumor-specifieke en geïndividualiseerde middelen om de informatievoorziening en zorg te verbeteren voor mensen die kanker hebben of hebben gehad, alsook hun naasten.

Ook **hoofdstuk 8** benadrukt het belang van zorg op maat voor kankeroverlevenden. Dit hoofdstuk beschrijft een clusteranalyse van nazorgbehoeften onder 292 Amerikanen die kanker hebben gehad met verschillende kankerdiagnoses. We laten zien dat de behoeften aan nazorg kunnen worden ingedeeld in 1) weinig of geen nazorgbehoeften (42%), 2) voornamelijk fysieke behoeften (16%), 3) voornamelijk psychologische behoeften (20%) en 4) zowel fysieke als psychologische behoeften (23%). In vergelijking met de eerste cluster waren degenen in de andere clusters jonger; degenen in de derde en vierde cluster rapporteerden meer psychologische problemen; en degenen in de tweede en vierde cluster rapporteerden meer vermoeidheid. Deze bevindingen laten zien dat de meerderheid van de mensen die kanker hebben gehad onvervulde behoefte aan nazorg heeft, maar dat tegelijkertijd een aanzienlijke groep weinig of geen nazorgbehoeften

heeft. Deze grote variatie in nazorgbehoeften toont aan dat het belangrijk is om informatievoorziening en zorg op maat aan te bieden. Daarnaast zou er wellicht rekening moeten worden gehouden met de nazorgbehoeften wanneer nazorginterventies zoals zorgplannen worden geëvalueerd.

Tot slot worden in **hoofdstuk 9** de veranderingen in tevredenheid met de informatievoorziening en zorg na terugkeer van kanker beschreven. Hiervoor werd data van de ROGY Care Studie gebruikt als prospectieve cohort. Gedurende twee jaar hebben 25 baarmoederkankerpatiënten (12%) en 64 eierstokkankerpatiënten (43%) een recidief gekregen, waarvan 9 baarmoederkanker- en 26 eierstokkankerpatiënten minstens één vragenlijst hebben ingevuld na vaststelling van het recidief. We laten zien dat patiënten ná vaststelling van een recidief minder tevreden waren over de zorg dan voordat het recidief werd vastgesteld, maar ook minder tevreden dan patiënten zonder recidief. Er was ontevredenheid over de sociale vaardigheden van de artsen, de uitwisseling van informatie tussen zorgverleners, maar ook de zorg in het algemeen. Deze bevindingen laten zien dat patiënten met een recidief behoefte hebben aan betere en passende zorg. Wellicht kan vroege palliatieve zorg hierin uitkomst bieden.

CONCLUSIE

Dit proefschrift laat zien dat zorgplannen waarschijnlijk niet zinvol zijn voor alle eierstok- en baarmoederkankerpatiënten, maar wellicht wel voor subgroepen, zoals patiënten die behoefte hebben aan een grote hoeveelheid informatie. Zorgplannen lijken daarentegen zelfs schadelijk te zijn voor patiënten die liever medische informatie vermijden. Deze resultaten wijzen erop dat zorgplannen veel meer afgestemd zouden moeten worden op de behoeften van de patiënt. Een aanvullend consult in het ziekenhuis zou, eventueel geleid door een verpleegkundig specialist, kunnen dienen om de informatie in het zorgplan te bespreken, de patiënt te ondersteunen in zijn of haar zelfmanagement en om te screenen op verdere informatie- en zorgbehoeften. Toekomstig onderzoek is nodig om (online) tools te ontwikkelen, waarmee informatie aangeboden kan worden die qua inhoud, type informatie en niveau van detail van de informatie gepersonaliseerd kan worden. Hiermee kunnen we de huidige richtlijnen in de kanker(na)zorg, verbeteren, en daarmee de (na)zorg voor mensen die kanker hebben of hebben gehad.

REFERENTIES

1. Torre LA, Siegel RL, Ward EM, Jemal A. Global cancer incidence and mortality rates and trends—an update. *Cancer Epidemiology and Prevention Biomarkers*. 2016;25(1):16-27.
2. Registry" NC. Incidentie alle tumoren. *Cijfers over Kanker* 2018; www.cijfersoverkanker.nl.
3. KWF. *Kanker in Nederland tot 2020, Trends en Prognoses*. 2011.
4. Registry" NC. Prevalentie alle tumoren. *Cijfers over Kanker* 2018; www.cijfersoverkanker.nl.
5. Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. *Cancer*. 2008;112(S11):2577-2592.
6. Harrington CB, Hansen JA, Moskowitz M, Todd BL, Feuerstein M. It's not over when it's over: long-term symptoms in cancer survivors—a systematic review. *The International Journal of Psychiatry in Medicine*. 2010;40(2):163-181.
7. Hewitt M, Greenfield S, Stovall E. From Cancer Patient to Cancer Survivor: Lost in Translation. Committee on Cancer Survivorship: Improving Quality Care and Quality of Life, National Cancer Policy Board. Washington, DC: National Academies Press; 2006.
8. Netherlands HCot. *Follow-up in oncology. Identify objectives, substantiate actions*. The Hague: Health Council of the Netherlands;2007.
9. Jacobsen PB. DA, Henderson TO., Mayer D., Moskowitz CS., Paskett ED., Rowland JH. Impact of cancer survivorship care plans (SCPs) on health outcomes and health care delivery: A systematic review. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2018;36, 2018 (suppl 7S; abstract 2).
10. van de Poll-Franse LV, Nicolaije KA, Vos MC, et al. The impact of a cancer Survivorship Care Plan on gynecological cancer patient and health care provider reported outcomes (ROGY Care): study protocol for a pragmatic cluster randomized controlled trial. *Trials*. 2011;12:256.
11. Ferrell B, Smith S, Cullinane C, Melancon C. Symptom concerns of women with ovarian cancer. *Journal of pain and symptom management*. Jun 2003;25(6):528-538.
12. Bradley S, Rose S, Lutgendorf S, Costanzo E, Anderson B. Quality of life and mental health in cervical and endometrial cancer survivors. *Gynecologic oncology*. 2006;100(3):479-486.
13. Abbott-Anderson K, Kwekkeboom KL. A systematic review of sexual concerns reported by gynecological cancer survivors. *Gynecologic oncology*. 2012;124(3):477-489.
14. Nicolaije KA, Ezendam NP, Vos MC, et al. Impact of an Automatically Generated Cancer Survivorship Care Plan on Patient-Reported Outcomes in Routine Clinical Practice: Longitudinal Outcomes of a Pragmatic, Cluster Randomized Trial. *Journal of Clinical Oncology*. 2015;33(31):3550-3559.

Publications

PUBLICATIONS INCLUDED IN THIS THESIS:

1. **de Rooij, B. H.,** Ezendam, N. P., Nicolaije, K. A., Vos, M. C., Pijnenborg, J. M., Boll, D., Kruitwagen, R. F. P. M. & Poll-Franse, L. V. (2016). Factors influencing implementation of a survivorship care plan—a quantitative process evaluation of the ROGY Care trial. *Journal of Cancer Survivorship, 1*(11), 64-73.

2. **de Rooij, B. H.,** Ezendam, N. P., Nicolaije, K. A., Vos, M. C., Pijnenborg, J. M., Boll, D., Boss, E. A., Hermans, R. H., Engelhart, K. C., Haartsen, J. E., Pijlman, B. M. & van de Poll-Franse, L. V. (2017). Effects of Survivorship Care Plans on patient reported outcomes in ovarian cancer during 2-year follow-up – The ROGY care trial. *Gynecologic oncology, 145*(2), 319-328.

3. **de Rooij, B. H.,** Ezendam, N. P., P., Vos, M. C., Pijnenborg, J. M., Boll, D., Kruitwagen, R. F. P. M. & van de Poll-Franse, L. V. Patients' information coping styles influece the benefit of a survivorship care plan in the ROGY Care trial: new insights for tailored delivery. *Cancer. In press*.

4. **de Rooij, B. H.,** Ezendam, N. P. M., Nicolaije, K. A., Lodder, P., Vos, M. C., Pijnenborg, J. M., Boll, D., Kruitwagen, R. F. P. M. & van de Poll-Franse, L. V. (2018). Survivorship care plans have a negative impact on long-term quality of life and anxiety through more threatening illness perceptions in gynecological cancer patients: the ROGY care trial. *Quality of Life Research, 27*(6), 1533-1544.

5. **de Rooij, B. H.,** Thong, M. S. Y., van Roij, J., Bonhof, C. S., Husson, O., Ezendam, N. P. M. (2018). Optimistic, pessimistic and realistic illness perceptions, quality of life and survival among 2457 cancer survivors: the population based PROFILES registry. Cancer, 124(7), 3609-17.

6. **de Rooij, B. H.,** Park, E. R., Perez, G. K., Rabin, J., Quain, K. M., Dizon, D. S., Post, K. E., Chinn, G. M., McDonough, A. L., Jimenez, R. B., van de Poll-Franse, L. V. & Peppercorn, J. (2018). Cluster Analysis Demonstrates the Need to Individualize Care for Cancer Survivors. *The Oncologist. Epub ahead of print.*

7. **de Rooij, B. H.*,** Thomas, T.H.*, Post, K. E., Flanagan, J., Ezendam, N. P. M., Peppercorn, J., Dizon, D. S. (2018). Survivorship care planning in gynecological oncology—perspectives from patients, caregivers and health care providers. *Journal of Cancer Survivorship. Epub ahead of print.*

8. **de Rooij, B. H.*,** Ikiz, H.*, Boll, D., Pijnenborg, J. M., Pijlman, B. M., Kruitwagen, R. F., van de Poll-Franse, L.V., & Ezendam, N. P. M. (2018). Recurrent Cancer Is Associated With Dissatisfaction With Care—A Longitudinal Analysis Among Ovarian and Endometrial Cancer Patients. *International Journal of Gynecological Cancer*, *28*(3), 614-622.

OTHER PUBLICATIONS:

1. Ramsey, I., **de Rooij, B. H.,** Mols, F., Horevoorts, N. J. E., Corsini, N., Eckert, M. & van de Poll-Franse, L. V. The impact of attrition on estimates of patient-reported, longitudinal health-related quality of life among colorectal cancer survivors participating in the PROFILES registry. *Submitted.*

2. Zandbergen, N., **de Rooij, B. H.,** P., Vos, M. C., Pijnenborg, J. M., Boll, D., Kruitwagen, R. F., van de Poll-Franse, L. V. & Ezendam, N. P. Changes in health-related quality of life among gynecologic cancer survivors during the two years after initial treatment: a longitudinal analysis. *Submitted.*

3. Husson, O., **de Rooij, B. H.,** Kieffer, J., Oerlemans, S., Mols, F., Aaronson, N., van der Graaf, W. T. A., van de Poll-Franse, L. V. Independent prognostic value of the EORTC QLQ-C30 summary score on all-cause mortality: Results from the population-based PROFILES registry. *Submitted.*

4. **de Rooij, B. H.,** Ezendam, N. P. M., Mols, F., Vissers, P. A. J., Thong, M. S. Y., Vlooswijk, C. C. P., Husson, O., Horevoorts, N. J. E. & van de Poll-Franse, L.V. (2018). Cancer survivors not participating in observational patient-reported outcome studies have a lower survival compared to participants: the population-based PROFILES registry. *Quality of Life Research. Epub ahead of print.*

5. Ezendam, N. P., **de Rooij, B. H.,** Kruitwagen, R. F., Creutzberg, C. L., van Loon, I., Boll, D., Vos, M.C. & van de Poll-Franse, L. V. (2018). ENdometrial cancer SURvivors' follow-up carE (ENSURE): Less is more? Evaluating patient satisfaction and cost-effectiveness of a reduced follow-up schedule: study protocol of a randomized controlled trial. *Trials*, *19*(1), 227.

*these authors contributed equally to this work

6. Camara, C., Vos, M. C., **de Rooij, B. H.,** Pijnenborg, J. M., Boll, D., van de Poll-Franse, L. V., & Ezendam, N. P. M. (2018). The role of positive psychological changes in anxiety and depression of patients with ovarian tumors and their partners: an observational study from the population-based PROFILES registry. *Supportive Care in Cancer*, 1-9.

7. **de Rooij, B. H.,** Ezendam, N. P. M. & van de Poll-Franse, L. V. Klachten en kwaliteit van leven bij (ex-)patiënten met een gynaecologische kanker (2017). *Reproductieve geneeskunde, Gynaecologie en Obstetrie anno 2017.*

8. Huibertse, L. J., van Eenbergen, M., **de Rooij, B. H.,** Bastiaens, M. T., Fossion, L. M., de la Fuente, R. B., Kil, P. J. Koldewijn, E. L., Meier, A. H. P., Mommers, R. J., Niemer, A. Q. & Ezendam, N. P. M. (2017). Cancer survivors' preference for follow-up care providers: a cross-sectional study from the population-based PROFILES-registry. *Acta Oncologica*, *56*(2), 278-287.

9. van Broekhoven, M. E., **de Rooij, B. H.,** Pijnenborg, J. M., Vos, M. C., Boll, D., Kruitwagen, R. F., van de Poll-Franse, L. V. & Ezendam, N. P. (2017). Illness perceptions and changes in lifestyle following a gynecological cancer diagnosis: A longitudinal analysis. *Gynecologic oncology*, *145*(2), 310-318.

10. **de Rooij, B. H.,** van der Berg, J. D., van der Kallen, C. J., Schram, M. T., Savelberg, H. H., Schaper, N. C., Dagnelie, P. C., Henry, R. M., Kroon, A. A., Stehouwer, C. D. & Koster, A. (2016). Physical activity and sedentary behavior in metabolically healthy versus unhealthy obese and non-obese individuals–the Maastricht study. *PloS one*, *11*(5), e0154358.

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About the author

Belle de Rooij was born on 28 February 1992 in Tilburg, the Netherlands. After graduating pre-university education at the St.-Odulphus Lyceum in Tilburg in 2010, she did a bachelor Health Sciences at Wageningen University, with part of her training at Corvinus University in Budapest, Hungary. After graduating her bachelor's degree in 2013, she did a Research Master in Health Sciences at Maastricht University, with a research internship at The Maastricht Study on obesity and the metabolic syndrome. In 2015, she completed her research master cum laude. Subsequently, she started her PhD research at Tilburg University and the Netherlands Comprehensive Cancer Organisation (IKNL). Her research focused on survivorship care planning for women with a gynecological cancer. As part of her PhD training, she did a 3-month research internship at Massachussets General Hospital, Harvard Medical School, in Boston, United States. Currently, she is working as a postdoctoral researcher at the IKNL and continues her research in the field of survivorship in gynecologic oncology.